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DYSPAREUNIA FOLLOWING VAGINAL OPERATIONS*

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APAREUNIA and dyspareunia are well accepted complications of operations which involve incision and suture of the vagina, and are variously explained. Some authorities emphasize the part played by tenderness of scars in the vaginal walls, others consider that shortening of the vagina, especially following vaginal hysterectomy, is an important factor. But the most obvious cause for post-operative dyspareunia is narrowing of the introitus and the vagina which results from removal of tissue as part of the cure of prolapse. Although these matters are often discussed, statements and opinions tend to be based on impressions so a factual examination of the incidence and causes of apareunia and dyspareunia following various vaginal operations may be of some interest.

MATERIAL

Since the occurrence of post-operative complications depends to some extent on differences in technique, skill and experience of individual operators, it was decided to confine the study to the results of operations carried out by one surgeon (T.N.A.J.). The operations were all performed not less than 2 years before the assessment of the result. Moreover, the assessment was made by personal interview and pelvic examination in every case. These examinations were conducted by one of us personally, with the assistance of Mr. Henry Roberts in the earlier part of the study. The series includes the sample of cases reported previously (Jeffcoate, 1959).

The case records of 385 consecutive women submitted to certain vaginal operations were examined and an attempt made to persuade each patient to attend for interview. One hundred and forty-two of the patients failed to attend, but 19 of these replied saying that they were well and completely satisfied with the result of the operation. These comments, however, are not included in our findings. The reasons for the non-attendance of the 142 women are shown in Table I.

TABLE I

Patients followed up		243
Patients not followed up		142
Died from incidental disease	4	
Poor general health prevented travelling	5	
Distance and inconvenience prevented attendance	118	
Not traced	15	
Total		385

* A paper presented by T. N. A. Jeffcoate to the South Western Obstetrical and Gynaecological Society, at Salisbury, 29th October, 1960.

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TABLE II

Anterior and posterior colpo-perineorrhaphy		177
With amputation of cervix	139	
With vaginal hysterectomy	36	
With previous hysterectomy	2	
Anterior colporrhaphy		44
With amputation of cervix	8	
With vaginal hysterectomy	19	
Vaginal hysterectomy alone		22
Total operations		243

The follow-up assessment is therefore limited to 243 women. These had been subjected, two or more years previously, to the types of operation shown in Table II.

ANTERIOR AND POSTERIOR COLPO-PERINEORRHAPHY

The established operative treatment for genital prolapse is anterior and posterior colpo-perineorrhaphy. Except in the young woman this double procedure is generally combined either with amputation of the cervix or with vaginal hysterectomy in order to secure access to the transverse cervical ligaments which are then tightened. One hundred and seventy-seven women in our series were treated by anterior and posterior colpo-perineorrhaphy. This was part of the Manchester operation in 139 cases, was combined with vaginal hysterectomy in 36 cases, and was carried out in patients previously subjected to abdominal total hysterectomy in 2 cases.

Thirty-seven of the patients could not be assessed symptomatically for subsequent coital function because 2 were single and 35 widowed. On examination, however, only one of these women had a vagina wide enough to permit coitus had they chosen to marry. Out of the 140 women with opportunities for coitus following operation, exactly half, namely 70, reported that coitus was being practised regularly and without discomfort; 8 of them had had pregnancies subsequent to the operation. There was, however good reason to believe that at least 4 of these women made misleading statements because, on examination, their vaginas were found to be so narrow that penetration during coitus would have been quite impossible.

The remaining 70 women reported apareunia or dyspareunia. Fifty-two of them had ceased or virtually ceased to practise coitus while 18 suffered considerable discomfort when it was attempted. It is at first sight remarkable that not less than 50 per cent women with opportunity fail to practise coitus, or only do so infrequently and with difficulty and pain, following anterior and posterior colpo-perineorrhaphy. It must, nevertheless, be recognized that this type of operation is often carried out in relatively old women who have ceased to have, or who are losing, any interest in physical sex. Thus, not less than 13 of the patients had not had coitus for several years before the operation, and at least 6 more had experienced progressive weakening of libido before and after the plastic procedure. Vaginal surgery in these cases did not appear to interfere with a natural progress of events. Nevertheless, there were many women who, at the time of operation, were relatively young and still leading a normal married life. Thus, out of the 70 patients with apareunia and dyspareunia, 29 were less than 50 years of age and only 21 were more than 60 years of age.

On examination, 43 of these 70 women were found to have the vulval introitus and vagina so narrowed that not more than one finger was admitted. In 13 of these the excessive narrowing was deliberately planned at operation with the intention of making certain of a cure, and in the knowledge that the patient was old and had long ceased to practise coitus. In the remainder, however, the surgeon had intended to leave a vagina capable of coital function.

In the 27 cases where the vagina appeared wide enough to permit coitus, other anatomical causes for dyspareunia were found as follows:

A long perineum making access difficult	2 cases
Stenosis of the upper vagina	3 cases
Shortening of the vagina	2 cases

There were, therefore, only 20 women with a genital canal which was anatomically satisfactory from the standpoint of comfortable coitus.

The determination of the basic cause of apareunia and dyspareunia in each case is not

TABLE III

Primary Causes of Apareunia and Dyspareunia Following Anterior and Posterior Colpo-perineorrhaphy

	Cases
Frigidity and impotence (male or female)	38
Stenosis of the vulva or vagina	19
Fear of injury	5
Vaginismus of uncertain aetiology	4
Shortening of the vagina	2
Tender cervical stump	1
Chronic urethritis	1

easy because more than one factor is often concerned. Thus atresia of the vagina and lack of libido frequently co-exist and one can be responsible for the other. Moreover, a complaint of pain may be made by the woman in order to cover lack of libido.

Our general conclusions in this respect, however, are shown in Table III. From this it will be seen that, in 38 out of the 70 cases, the fundamental cause for apareunia was frigidity or impotence on the part of one or both of the marital partners. This condition was present before operation in the majority of cases but in some it was a gradual phenomenon occurring partly before and partly after operation. In at least 7 cases its cause was serious illness of either husband or wife.

There were 9 cases in which the anatomy of the vagina was satisfactory and in which apareunia or dyspareunia was due to psychological factors. In 5 of these either the wife or the husband was afraid that coitus would cause injury and bring about a recurrence of prolapse; in 4 the nature of the fear or nervous tension which caused vaginismus in the wife was less certain. There was only one case in which dyspareunia was caused by scarring and tenderness around the cervical stump, and only two in which shortness of the vagina appeared to be the cause of the trouble. In one of these latter the uterus had been removed previously by the abdominal route, in the second the Manchester operation had been performed.

In not less than 19 of the cases the main source of the trouble was that the vulva and vagina were too narrow to admit penetration. It is not suggested that this narrowness was necessarily present at the conclusion of the operation; the operation notes sometimes made a specific comment to the contrary. What so often happened in these cases was that the patient delayed resuming married life for some considerable time after operation and then, when attempts at coitus were made, dyspareunia was experienced and further attempts abandoned. The narrowness was therefore in large measure accounted for by disuse atrophy and senile change.

From these findings it would appear that, although 50 per cent women suffered failure of married life following anterior and posterior colpo-perineorrhaphy, many did not mind because they and their husbands no longer had any interest in sex. There were, however, not less than 30 out of the 70 women, some of them comparatively young, who regretted the loss of this function. This represents approximately 20 per cent of all women who, having been subjected to this type of operation, agreed to follow-up examination.

THE CAUSE OF VAGINAL STENOSIS

The main avoidable cause for apareunia and dyspareunia following anterior and posterior colpo-perineorrhaphy is excessive narrowing of the vaginal lumen and closure of the vulval introitus. The factors concerned in this excessive narrowing are several.

(1) *Deliberate Narrowing of Vagina by the Surgeon*

When a woman is old and no longer practising coitus the calibre of the vagina is often purposefully reduced by the surgeon in order to obtain a good result. This may be necessary in those cases of genital prolapse in which the vagina is short, or in which the supports of all the pelvic organs are weak. Nulliparous prolapse, for example, may be difficult to cure without grossly reducing the size of the vagina.

(2) *Misjudgment by the Surgeon*

The narrowing sometimes occurs because the surgeon misjudges the amount of vaginal wall to be removed and over-tightens the underlying muscles and fascia. This can reflect surgical inexperience but more often happens because

no allowance is made for the subsequent spontaneous involution of over-stretched tissues, and for impending climacteric changes in the vagina. There are two especially important points in surgical technique. Firstly, the classical Hegar's triangular incision for posterior colpo-perineorrhaphy results in a constriction about one inch above the perineum; the posterior incision is better shaped like an inverted T. Secondly, extension of the incision on to the labia majora to close the introitus by vulvo-orrhaphy (Robinson, 1934) is to be avoided.

(3) *Senile Contracture*

The genital atrophy which follows the climacteric change normally results in gradual closure of the vagina and introitus. So the gaping vulva and patulous vagina of the multiparous woman aged 40 years can, by the time she is 70 years of age, become quite a narrow tube. This physiological change is only arrested or controlled by the regular practice of coitus. If any post-menopausal woman discontinues coitus for any length of time she finds its resumption difficult if not impossible.

(4) *Failure to Practise Coitus*

A vaginal plastic operation not only interrupts the practice of coitus; it often leaves the woman with a tender perineum and an introitus much smaller than she or her husband expected. Initial dyspareunia is therefore almost inevitable. The younger couple with strong sex urges generally overcome this difficulty and all is well. In the woman of menopausal or post-menopausal age, however, a less satisfactory outcome is common. If she avoids coitus until all tenderness subsides, senile contracture is given an opportunity to operate. If she attempts it too early, pain and vaginismus act as a deterrent for several weeks or months. Meanwhile the vagina continues to shrink so that later efforts, made perhaps rather fearfully lest pain or injury result, also fail. Sex desire is in any case weakening so the reaction of both husband and wife is not to try again. Thus apareunia persists and the introitus and vagina become more and more stenosed.

The prevention of apareunia and dyspareunia following operations for prolapse therefore demands—(*i*) that the introitus and lower vagina are not constricted; (*ii*) that the introitus is not left so tender as to make the couple postpone unduly the resumption of coitus. Both these objects can be best achieved by omitting posterior colpo-perineorrhaphy wherever possible.

Anterior Colporrhaphy without Posterior Colpo-perineorrhaphy

To test the above conclusion, the results of operations for prolapse which did not include posterior colpo-perineorrhaphy were examined. The series of cases followed up was smaller and numbered only 44 (Table II). This is because, in conformity with general practice, posterior colpo-perineorrhaphy was not omitted from prolapse operations until comparatively recently and two years had to elapse before the assessment of the results. We now avoid this procedure much more frequently.

Four of the women examined were widowed or single so there were only 40 in whom coital function could be assessed. Twenty-three of these reported that coitus took place regularly and without discomfort and, when examined, were found to have a satisfactory anatomical result of the operation. Although all were less than 60, and the majority less than 50, years old at the time of operation, 6 patients reported complete apareunia and 3 practised coitus very infrequently. In 6 out of these 9 cases the trouble was frigidity and impotence affecting one or both partners and present before the operation. In the remaining three, coitus was avoided because it induced stress incontinence of urine (one case), because of fear of injury (one case), and because of pain arising from a tender cervical stump (one case). On examination, the vagina was found to admit two fingers in all 9 cases and there was no anatomical reason for dyspareunia except in the one in which there was tenderness and scarring around the cervical stump.

Eight women reported that coitus took place but caused discomfort. In all these, examination showed that the lumen of the vagina was adequate. In one, however, the upper vagina was constricted by adhesions around the cervix and in a second the vagina was unusually short.

The latter may have been a developmental defect but another possible explanation is the fact that the patient has previously had a repair operation in another hospital and the anterior colporrhaphy was carried out for recurrent prolapse. In neither of these cases, however, did the anatomical defect appear to explain the dyspareunia. Indeed, in 7 out of the 8 cases the cause of dyspareunia was vaginismus; this pre-existed the operation in 2 cases, was associated with frigidity in 4 cases, and with fear that coitus would do damage to the operation field in one case. The eighth patient said that the discomfort appeared to be due to shortness of the vagina but there was no evidence of this on examination.

Our final assessment of the basic causes for apareunia and dyspareunia in this group is shown in Table IV.

It is remarkable that in this admittedly small series of married women there was none in whom the lumen of the vagina had been reduced too much by the operation. Apareunia and dyspareunia always had another explanation.

Posterior Colpo-perineorrhaphy without Other Procedures

During the years under review posterior colpo-perineorrhaphy alone was rarely performed. This is because deficiency of the perineum was never regarded by itself as an indication for operation, and also because rectocele is not often seen by itself. Even when repair of a complete perineal tear was included, the number of cases of posterior colpo-perineorrhaphy was too small to permit statistical evaluation.

Table IV

Primary Cause of Apareunia and Dyspareunia Following Anterior Colporrhaphy

	Cases
Frigidity and impotence (male and female) ..	10
Vaginismus pre-existing operation	2
Fear of injury	2
Stress incontinence of urine	1
Tender cervical stump	1
? Shortness of vagina	1
Total	17

The commonest time at which repair of posterior vaginal wall and perineum is carried out without any other procedure is, of course, immediately after childbirth. And it may be noted that dyspareunia, persisting for at least a few weeks or months, is by no means uncommon after obstetrical perineorrhaphy. There is a tendency to repair perineal tears and episiotomy incisions too tightly and to disturb the anatomy of the vagino-perineal junction. At this junction itself it is often best not to insert any sutures but, having stitched the vagina above and the perineum behind, to allow the tissues between to take up their own natural position for healing.

The Disadvantages of Posterior Colpo-perineorrhaphy

Posterior colpo-perineorrhaphy not only has the disadvantage of narrowing the lower vagina and introitus. It accounts for most of the discomfort experienced by the patient after vaginal operations. Anterior colporrhaphy alone, and even vaginal hysterectomy, cause practically no post-operative pain. The perineal skin, however, is extremely sensitive while the stitching of the deep perineal muscles causes intense deep-seated discomfort for many days. Indeed the tenderness may persist for several weeks. A third disadvantage of posterior colpo-perineorrhaphy is its proneness to cause post-operative retention of urine with a train of complications such as incomplete emptying of the bladder and cystitis. Anterior colporrhaphy is much less likely to interfere with bladder function except when it is combined with urethroplasty aimed to cure stress incontinence. Perineorrhaphy causes retention of urine because the spasm of the levatores ani muscles induces a sympathetic spasm in the voluntary external urethral sphincter (Francis, 1960).

There are, therefore, good reasons for avoiding posterior colpo-perineorrhaphy whenever possible, and also for questioning why it has come to occupy such an important place in gynaecological surgery. This place is explained by the history of operations for prolapse and has been set out in detail elsewhere (Jeffcoate, 1959). In brief, repair of the perineum was first

carried out in the hope of curing complete perineal tears. From this it was extended in an attempt to cure uterine prolapse and cystocele. For this purpose it is as old if not older than anterior colporrhaphy. Although it was soon clear that perineorrhaphy, and subsequently posterior colpo-perineorrhaphy, did not cure any prolapse except rectocele, it continued to be carried out in the 19th century because it was the only operation which was technically possible. In order to justify its performance the surgeons therefore created the anatomical concept that the vaginal walls are supported by the perineum and that the uterus is in turn supported by the vagina. This theory, for which there is no favourable and much unfavourable evidence, is still passively accepted if not actively enunciated by many gynaecologists. Hence statements to the effect that a cystocele should never be repaired nor the uterus removed vaginally without the perineum being simultaneously reconstituted.

The idea that the perineum is important in supporting the female genitalia became so deeply ingrained that even Fothergill did not have the courage to abandon posterior colpo-perineorrhaphy. Thus, in his description of his operation, and knowing that the uterus is supported by the transverse cervical ligaments, he wrote, "To complete the operation the vaginal outlet is narrowed by repairing the perineum. The upper part of the posterior part of the vaginal wall is not touched" (Fothergill, 1913).

If present-day views regarding the anatomical supports of the vagina and uterus are correct, posterior colpo-perineorrhaphy has no place in the treatment of cystocele and uterine prolapse —except it be used to hide from onlookers the prolapse which still persists after inadequate surgery around the vaginal vault and upper anterior vaginal wall. That the omission of the posterior repair does not prejudice the result of vaginal plastic operations is shown by a study of the prolapse recurrence rate in our cases.

Recurrence of Prolapse

Amongst the 44 patients who were treated for genital prolapse by anterior colporrhaphy with amputation of the cervix or vaginal hysterectomy, the findings on follow-up examination were as follows:

Slight symptomless cystocele ..	2 cases
Slight cystocele with symptoms	2 cases
Slight symptomless rectocele ..	1 case
No prolapse of any kind ..	39 cases

Of the 2 women with cystocele and symptoms, one suffered from chronic bronchitis, and the other had undertaken heavy manual labour commencing 6 weeks after operation and continuing until the time of examination. Neither patient has required further surgery as yet.

Among the 177 women treated by posterior colpo-perineorrhaphy as well as anterior colporrhaphy, prolapse recurred as follows:

Slight symptomless cystocele ..	6 cases
Slight cystocele with symptoms	3 cases
Uterine prolapse and cystocele with symptoms	1 case
Slight symptomless enterocele	1 case
No prolapse of any kind ..	166 cases

From these findings it would appear that there is not a significant difference in the recurrence rate in the two groups.

It might next be asked what happens in those cases where the uterus is removed vaginally for conditions other than prolapse, and where the residual vagina is not protected by simultaneous posterior colpo-perineorrhaphy. A series of 22 patients subjected to this type of operation more than 2 years previously were examined. Two were noted to have a slight rectocele but this was symptomless and the women were well pleased with the result of the operation. One patient, however, gave a history of having had some sort of plastic procedure carried out in another hospital. The reason for this is unknown but what is known is that the subsequent repair resulted in a very narrow vagina causing apareunia. In none of the remaining 19 cases was there any sign of prolapse. Here again, the findings suggest that vaginal hysterectomy, if carried out with proper attention to the tissues at the vaginal vault, carries no special risk of subsequent vaginal prolapse even if posterior colpo-perineorrhaphy is omitted.

For comparison with the other series of cases, coital function following vaginal hysterectomy

without colporrhaphy was also studied. Of the 22 women, one was single and 6 were widowed. One of the widows, however, had had normal coitus post-operatively for several years prior to her husband's death. On examination of these widows it was noted that the vaginal lumen varied with age and the degree of senile atrophy. In 2 the length was shortened because the operation had been carried out for carcinoma of the body of the uterus and a liberal cuff of vagina had been removed.

There were 15 patients who had opportunities for coitus following vaginal hysterectomy and 8 of these reported regular and comfortable intercourse. One, already mentioned, had subsequently had a repair operation elsewhere and then suffered apareunia. It is remarkable, however, that of the 15 patients with opportunities, 6 never practised coitus at all and half of these were less than 50 years of age at the time of operation. All these 7 had a normal vagina anatomically except for one elderly woman who showed some senile contracture. The cause for the apareunia in all cases was impotence of the husband or absence of libido in husband and wife; these represented progressive developments throughout many years and were not directly related to the operation. The last patient in the series suffered from dyspareunia which appeared to be due to vaginismus present both before and after vaginal hysterectomy.

The Surgical Treatment of Prolapse

The above considerations lead to certain conclusions in regard to the surgical treatment of genital prolapse. For cystocele anterior colporrhaphy is clearly necessary. For uterine prolapse the essential is to define and shorten the transverse cervical ligaments, combining this with upper anterior colporrhaphy. Whether the transverse cervical ligaments are exposed by way of amputating the cervix or by vaginal hysterectomy is a more controversial matter. We recognize a place for both procedures although vaginal hysterectomy is reserved for special circumstances. Whichever is chosen, however, any redundant peritoneum of the pouch of Douglas should be excised and the underlying fascial tissues strengthened. This means that the pouch of Douglas should be opened in every operation of any type which is carried out for uterine prolapse. It is this procedure, however, which can cause narrowing of the upper vagina unless care is taken. Indeed, in certain cases of large enterocele, it may be impossible to avoid a certain degree of contracture at the vault. This, however, should not matter materially providing the calibre of the lower vagina remains adequate.

Once the suturing in and around the cervix, the vaginal vault and the upper half of the anterior vaginal wall is complete, the operation for uterine prolapse is complete. Posterior colpoperineorrhaphy can in no way improve the result. Indeed, the only clear indication for this procedure is the presence of a significant degree of rectocele. Enterocele requires not repair of the perineum and the lower vaginal wall but strengthening of the upper vaginal wall and vault; this is best done at the time the cervix is amputated or the uterus removed.

Those who carry out posterior colpoperineorrhaphy frequently and routinely tend to justify the procedure by the finding of what is generally called a deficient or defective perineum. The deficiency may represent the failure of a perineal tear to heal by first intention, or it may consist of nothing more than atonicity of the perineal muscles beneath an intact skin. In fact, a defective perineum by itself rarely causes any symptoms. Colpo-perineorrhaphy may be necessary when gross laxity of the introitus interferes with orgasm, or when it causes vaginal flatus, but these are quite exceptional complaints. The perineal deficiency which the surgeon usually demonstrates at the conclusion of anterior colporrhaphy is generally an artefact. It is mostly the result of relaxation of the perineal muscles induced by general anaesthesia and, now-a-days, by the administration of relaxant drugs. It is, therefore, important that the state of the perineum and the presence or absence of rectocele be assessed before the patient is anaesthetized and prepared for operation. We have for several years made it a rule to say, at the time an operation is being planned, whether or not posterior repair is required. And, having made the decision, the opinion is not changed at the time of operation itself.

In making the pre-operative assessment, it is to be recognized that some gaping of the vulva is probably normal in the multiparous woman in her thirties and forties. Reproduction under natural conditions, that is, without skilled attendants, probably causes some degree of perineal weakening or tearing during all first labours. The resulting perineal deficiency then permits easy exit of subsequent babies but is ultimately corrected by climacteric atrophy which restores the introitus to its nulliparous dimensions. So, whenever the surgeon decides that posterior colpo-perineorrhaphy is necessary it is important to allow for this subsequent atrophy, to limit the removal of the lower vaginal wall and to avoid lengthening the perineum to close the introitus. In those women who have ceased to practise coitus, narrowing of the vagina is of no account. In women still living a normal married life, and in widows who may re-marry, caution is required. It thus becomes necessary to enquire about coital function before operation in every case. Failure to do this can be disconcerting for the surgeon. In one of our cases a woman aged 62 years was subjected to the Manchester operation. In the knowledge that her husband was a decrepit retired business man aged 73 years, and because the vagina was comparatively short, the genital tract was deliberately narrowed at operation. It was her husband who subsequently complained most bitterly.

Coital Function Before Operation

The practice of coitus both before and after vaginal operations is to a considerable extent governed by the ages and health of the partners in marriage. In this connexion Turnbull (1955) found that the sex urge is waning in 60 per cent of women before the menopause and, in half of these, shows a further weakening soon after the menopause. Only 30 per cent women in his series retained strong or moderately strong libido after the climacteric. This is only one side of the problem and the husband, too, has to be considered. Indeed, Kinsey *et al.* (1953) found that it is decline in the husband's sex interest which often accounts for the change in female libido with age.

The retrospective study of cases reported here shows that not less than 25 per cent married women had completely ceased to practise coitus by the time they were submitted to repair operations or to vaginal hysterectomy. This is because they were often more than 40 years of age and the sex urge of either husband or wife had failed. Sometimes the presence of prolapse acted as a pre-operative deterrent, sometimes disinterest in sex was associated with hard work, pre-occupation with domestic responsibilities and a lack of desire for further children. Not infrequently, general ill health of one or other partner played a part. The study also shows, however, that it is impossible to generalize and to assume that old age necessarily means cessation of married life. Each case has to be treated individually.

During the last year an attempt was made to assess coital function pre-operatively in all women admitted to our unit for vaginal hysterectomy or repair of prolapse. There were 109 cases. Information was not obtained from 16, in one case because the patient refused to give it, in the others because the person conducting the enquiry (W.J.A.F.) was not available when the patient was admitted. Of the remaining 93 women, 20 were widowed or separated so the findings shown in Table V concern only 73 married couples.

This prospective study confirms the retrospective analysis in that it shows that approximately 25 per cent women cease to practise coitus before the operations under consideration. And it also indicates that coitus is continued regularly until old age in certain cases. Thus

Table V

Coital Function Before Vaginal Operations

Age	21–30 Years	31–40 Years	41–50 Years	51–60 Years	61–70 Years	Total
Coitus discontinued	–	–	4	6	8	18
Infrequent coitus ..	–	1	7	9	1	18
Regular coitus ..	4	10	15	7	1	37
Totals ..	4	11	26	22	10	73

TABLE VI

Pre-operative Failure to Practise Coitus Regularly

Causes	
Decreased libido	13
Ill-health of wife	8*
Ill-health of husband	4
Presence of prolapse	6*
Functional dyspareunia	3
Defective perineum—male dissatisfaction	1
Uterine haemorrhage	1

* Failing libido also a factor in 5 of these cases.

one-third of women aged 51 to 60 years were living a normal married life and another one-third practised coitus occasionally. The causes for the absence or infrequency of coitus in this series are of some interest and are shown in Table VI. In this the decreased libido is credited to the wife although it has to be recognized that it often reflects a failure in the sex interest of the husband. It is also noticeable that in certain cases the indication for the operation was the cause of failure to practise coitus so there was hope that treatment would improve married life. In a few cases we already know that this has happened.

POST-OPERATIVE CARE

Analysis of the cases of apareunia and dyspareunia following vaginal operations suggests that the trouble is sometimes avoidable by post-operative care and education of the patient. The formation of adhesions between the anterior and posterior vaginal walls, even when the incision is limited to the anterior wall, is not uncommon. These are revealed by routine vaginal examination 2 to 3 weeks after operation; they are easily separated at that time and do not generally re-form. Nevertheless, a further examination 6 weeks after operation should be a regular practice. Meticulous care over these two post-operative examinations explains why vaginal adhesions do not appear as a cause for dyspareunia in our series. There were only two cases in which adhesions below the level of the cervix were found later than 3 weeks after operation. In one the woman was very old and no longer practising coitus so the finding was of little account. In the other an adhesion did cause initial dyspareunia but this was soon cured by division of the band under general anaesthesia.

Education of the patient is concerned with sex. She should be advised not to practise coitus until the examination at 6 weeks shows that the wounds are healed and free from tenderness. Whereupon, she should be specifically told to resume married life. Both husband and wife also require reassurance that coitus, even if at first a little difficult, will not impair the result of the operation and that its undue deferment may result in apareunia from climacteric contracture.

OTHER TENDER SCARS AND SHORTENING OF THE VAGINA

It is sometimes stated that a common cause of dyspareunia following vaginal operations is that the scars remain painful and tender. In our experience this is extremely rare. Indeed, there was not one case in which tenderness of the vaginal scars was the cause of pain or difficulty. Moreover, there were only 2 patients in whom dyspareunia was attributable to tenderness and fixation of the cervical stump after amputation; in these vaginal hysterectomy might have avoided the trouble although this operation is alleged to have the disadvantage of shortening the vagina. But even this statement is not supported by our observations. Functional shortening of the vagina was found in 4 cases and was due to narrowing of the upper vagina in the course of amputation of the cervix, cure of enterocele and upper anterior colporrhaphy. Actual shortening was noted in 6 cases, once after the Manchester operation, once after anterior and posterior colporrhaphy following previous abdominal hysterectomy, once after anterior colporrhaphy following a failed Manchester repair and thrice after vaginal hysterectomy. In 2 of these last cases the shortening of the vagina was explained by the removal of a large vaginal cuff as part of a radical approach to the treatment of carcinoma of the body of the uterus. And here it may be noted that, in all, there were 77 women subjected to vaginal hysterectomy with or without colporrhaphy.

Only 2 of the 10 women with absolute or functional shortening of the vagina complained of dyspareunia. There was one other case in which pain was alleged to be due to a short vagina but on examination the length appeared adequate.

The conclusion is that, given reasonable attention to technique, unintentional shortening of the vagina rarely results from either vaginal hysterectomy or colporrhaphy and, when it does, the question always arises as to whether the shortness preceded the operation. The vagina varies in length, and developmental shortness is probably a predisposing factor in causing uterine prolapse. One of the objects of any operation should therefore be to lengthen the vagina. This can usually but not always be achieved.

Summary and Conclusions

Apareunia and dyspareunia are commonly found after operations for prolapse. Approximately 50 per cent women do not practise coitus at all or do so infrequently and with discomfort following operations of this type. In half of these, however, the explanation is loss of libido on the part of husband or wife and sometimes definite impotence. These symptoms are generally a manifestation of advancing years or deterioration in health and are often present before the operation. Indeed, 25 per cent of married women subjected to repair operations or vaginal hysterectomy have, for various reasons, ceased to have coitus before operation.

A certain number of patients avoid coitus following these operations because they are afraid that harm will result.

Approximately 20 per cent of women who have repair operations for prolapse subsequently suffer apareunia or dyspareunia because the vagina is too narrow. This narrowing is partly due to senile atrophy, a normal physiological process, and partly because posterior colpo-perineorrhaphy is combined with anterior colporrhaphy. Posterior colpo-perineorrhaphy should therefore be avoided in all cases except where there is a clear indication such as the presence of a demonstrable and symptom-causing rectocele. Even then the amount of tissue removed should be judged in relation to the fact that the patient is at an age when senile atrophy will supervene in the ensuing few years.

Shortening of the vagina and tender scars, resulting from repair operations and from vaginal hysterectomy, are not significant causes of post-operative dyspareunia. If care is taken, shortening of the vagina can be generally avoided but difficulty can arise because women with uterine prolapse sometimes have congenitally short vaginas.

Vaginal adhesions should be broken down 2 to 3 weeks after operation and, 6 weeks after operation, the patient should be re-examined and then given specific instructions about the resumption of coitus.

Attention to these points offers a prospect of reducing the incidence of post-operative dyspareunia by approximately 50 per cent.

The series reported here extends over several years. The incidence of apareunia and dyspareunia was higher in the earlier than in the later cases because it is only with increasing experience that the considerations here put forward were appreciated.

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THE MECHANISM OF RHESUS ISO-IMMUNIZATION

BY

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HAEMOLYTIC disease of the newborn due to Rh-immunization occurs, with few exceptions, in the second or later Rh-positive foetuses of Rh-negative women. But it is known that only a small proportion of foetuses so specified are in fact affected. The factors determining the occurrence of the disease in this small proportion have not yet been identified. At a time when improvements in the management of haemolytic disease are giving diminishing returns it is important that these factors should be investigated energetically since a better understanding of their nature offers the hope of reducing the incidence of the disease and possibly preventing it. This paper is the third in a series of studies in which we have examined the detailed nature of these factors.

In the first paper (Knox and Walker, 1957) we analyzed the birth rank distribution of infants first affected in their families and inferred the existence of an important factor not present at the time of marriage and therefore not genetic. We also concluded that it was associated with either the sensitizing or the immunizing pregnancy, but not both; we could not, from our data, distinguish which pregnancy it was. The frequency of occurrence of this factor was about one in seventeen pregnancies.

We recognized at the time that there was a reduced incidence of ABO heterospecificity among affected children but, since only one-fifth of all pregnancies in this country are ABO heterospecific,* we regarded it as an unimportant factor quantitatively.

Later, however (Knox, Murray and Walker, 1960), our attention returned to ABO heterospecificity for a different reason. We realized that, if we could identify the pregnancy in which ABO heterospecificity protected, we had also identified the site of the factor against which it protected. A study of the relative frequencies of ABO heterospecificity in sensitizing† and immunizing† pregnancies showed that the adventitious factor was at the sensitizing pregnancy.

The present investigation was designed to confirm this directly if possible, by demonstrating differences between the details of a series of known sensitizing pregnancies and a series of control pregnancies. It was also hoped to identify the factors responsible for sensitization. This, we believe, has in large part been achieved.

* We used this term to indicate the presence in the foetus of A or B antigen and the presence in the mother of the antibody to that substance.

† We used the term "immunizing pregnancy" to indicate the pregnancy during which antibodies and a diseased child first appeared—sensitizing pregnancy to mean an earlier Rh-positive pregnancy (not necessarily identified precisely) during which the ability to develop immunity later, was determined.

Material and Methods

We collected data from families in which the first infant was known to be normal and the second one affected, since in these families we have the simplest possible situation and the most certain identification of the sensitizing pregnancies. Over 200 such families in our records were written to and the place of birth of the first (i.e., normal) infant ascertained.

They were widely scattered both at home and in a large number of hospitals and maternity homes, locally and in other parts of the country, and over a long period of time. The practical difficulties of finding adequate antenatal and obstetric records and a suitable paired control case compelled us to concentrate on the recent records of a small number of local hospitals. We thus obtained a relatively small series for analysis consisting of 44 cases together with an equal number of controls. A control was the primiparous delivery nearest in the hospital records. To avoid unconscious bias and the effects of any systematic changes in time, it was laid down that, if the index case had an even serial number, the subsequent case was used as a control and, if an odd number, the previous case. In most maternity units the records were stored chronologically in order of their serial admission numbers, but in one unit, where the records of each separate year were arranged alphabetically, we still used the adjacent case as stored.

Data were extracted on to prepared schedules which, since we did not know in advance the degree and variation of detail to expect, were designed to record a greater complexity of information than we actually found. However, we obtained systematically the mother's age and her obstetric, transfusion and medical histories; the details of pregnancy including duration, abnormalities, obstetric procedures, and blood pressures; the duration, abnormalities and procedures of the different stages of labour; information regarding the foetus, placenta, and progress during the puerperium.

Finally, for a purpose we shall refer to later, we scrutinized the obstetric records at one hospital to obtain a series of 50 Rh-negative primiparous women, and from each of these records we extracted the highest diastolic blood pressure recorded before the onset of labour.

Results

Of the 44 index cases traced we found that one had been given in error a transfusion of Rh-positive blood for post-partum haemorrhage. Another had had an Rh-negative infant at the first pregnancy and we attributed her sensitization to a transfusion of unknown group given as a child in association with a thoracotomy. These two cases and their controls were excluded from the subsequent analysis.

Maternal Age and Previous History

The mean recorded age of the mothers at the time of delivery was 24·57 years in the index series, and 25·36 years in the control series. The difference between these means is not statistically significant. It is worth the comment here, however, that we did not necessarily expect the two series to be perfectly matched by age since the index series were all selected through having had a second infant and may have had their first infants at a relatively early age when compared with a randomly selected group of first infants. This imperfection of matching had to be remembered also with respect to other comparisons between the groups but did not seem likely to affect any of the conclusions, and in practical terms it was unavoidable.

Two of the index cases had reported a previous abortion or miscarriage compared with 4 of the controls. The methods of treating these miscarriages were not recorded. Apart from these events there were no other previous obstetric events or procedures in either group. We detected no differences in the frequency or nature of previous recorded illnesses, most of which were trivial. Duration of marriage was not recorded with sufficient consistency for formal analysis.

Duration of Pregnancy

The date of onset of the last menstrual period (and/or the calculated expected date of delivery) and the actual date of delivery were recorded sufficiently consistently to derive an estimate of days premature (−) or days overdue (+) in all but 4 cases. They ranged from −58 to +54 days.

The mean figures were −3·3 for index cases and +1·2 for the controls. Five of the index cases and 4 of the controls were artificially induced or had Caesarean section before the onset of labour, and if these cases are excluded the mean figures for spontaneous deliveries are −1·2 and +1·4 days respectively. This is not significant.

The distributions were also essentially similar in that there were 4 children in each group delivered 14 or more days later than expected and 4 index against 2 controls delivered spontaneously 21 or more days early.

Toxaemia of Pregnancy

Oedema (of any site) was recorded in 14 index cases (33 per cent) against 2 controls (5 per cent) a difference which is statistically significant ($\chi^2_{(1)}=4·26$, $P<0·05$).

Two of the index cases and none of the controls were admitted for bed rest in hospital. One of the index cases had eclamptic fits.

Systolic and diastolic blood pressures were recorded in almost all cases and the highest record of each at any time before the onset of labour was used for analysis. The systolic and diastolic readings used were not necessarily on the same occasion. The grouped readings are set out in Tables I and II.

The systolic pressures of the index pregnancies were at or above the approximate median value of 135 more often than in the control group but the difference is not statistically significant ($\chi^2_{(1)}=2·91$, $P=0·1–0·05$).

The diastolic pressures show the same trend but provide much more convincing evidence of a true difference. The trend is systematic with changing pressure and the variance-ratio test shows that it is significant at the one-per-cent level.

We consider, therefore, that there is convincing evidence of an association between Rh sensitization and toxaemia of pregnancy as measured by the presence of oedema and a raised diastolic blood pressure and that the risk of sensitization rises with increasing severity of the toxaemia.

Duration of Labour

We compared the groups in respect of each stage of labour separately.

The mean duration of the first stage, in women allowed to complete the first stage, was 12·55 hours in the index cases and 13·98 hours in the controls. The range was 2 hours to 52 hours and the difference of 1·43 hours (86 minutes) was not statistically significant. When index cases were compared with their individual paired

TABLE I

Maximum Antenatal Systolic Blood Pressures in Sensitizing Pregnancies and in Controls

	Mm. of Mercury								Total	Mean
	110–	120–	130–	140–	150–	160–	170–	180–		
Sensitizing pregnancies	2	6	17	6	2	4	0	1	38	139·5
Controls	4	12	13	6	2	1	1	0	39	134·2

$F=2·68$: $P>0·05$.

TABLE II

Maximum Antenatal Diastolic Blood Pressures in Sensitizing Pregnancies and in Controls

	Mm. of Mercury						Total	Mean
	–74	75–	85–	95–	105–	115–		
Sensitizing pregnancies	3	9	14	8	2	2	38	90·8
Controls	5	19	12	3	0	0	39	83·3

$F=10·22$: $P<0·01$.

controls (incomplete pairs excluded), 17 had longer and 18 shorter first stages.

Second stages ranged from 10 to 250 minutes and the means for index and control groups respectively were 58·9 minutes and 60·3 minutes. There is no suggestion of a difference here. However, it is possible that a precipitate second stage may have some association with sensitization since 5 index cases and no controls had second stages of 15 minutes or less ($p=1/16$, or 1/32 single-tailed). There was no suggestion of differences in the upper range duration.

Analysis of the second stage was complicated by the fact that 7 index cases and 9 controls were delivered with forceps. Only 2 of these 16 were delivered within an hour of onset of the second stage and 7 were not delivered until after 2 hours. However, detailed inspection of the data did not reveal any differences between index and control groups other than the one already mentioned.

Third stages were usually recorded in multiples of five minutes but the recorded limits were 2 to 120 minutes. Taking each record to the nearest multiple of 5 and truncating the distribution at 60 minutes, the mean for the index cases was 18·9 minutes and 17·5 minutes for the controls. Nor was there evidence of any other difference between the distributions although, once more, the matter was complicated by surgical interference, in this stage consisting of 4 index cases where manual removal of the placenta was performed.

Obstetric Procedures

These are given in Table III and are arranged in two groups. There was no real difference in the frequency of procedures which seemed unlikely to disturb the chorio-decidual junction, but there were 15 procedures in the index cases, against 4 in the controls, of a kind likely to disturb this junction. Some women had more than one of these procedures and when women rather than procedures were counted, the ratio was 13 to 4. This is statistically significant ($\chi^2_{(1)}=4·76$, $P<0·05$).

Blood loss was recorded irregularly, sometimes in ounces, sometimes only in descriptive terms such as "normal", "average", "little" or "free", but because each pair of cases came from the same hospital at the same time it was often possible to say that the index case bled more than the paired control or vice versa. Of 24 pairs where such a statement proved possible, 12 index cases bled more than their controls and 12 bled less. Two index cases and 2 controls had blood transfusion.

TABLE III
Obstetric Procedures

	Index Cases	Control Cases
(*a*) Procedures likely to disturb the chorio-decidual junction:		
External version	3	0
Surgical induction	5	1
Caesarean section	3	2
Manual removal of placenta	4	0
Credé's expression of placenta	0	1
	15	4
(*b*) Procedures not likely to disturb the chorio-decidual junction:		
Correction of retroversion ..	1	0
Medical induction	0	1
Forceps delivery	7	9
	8	10

Most women in both groups had episiotomy performed and others had perineal laceration alone or in addition to episiotomy but there were no evident differences between the groups in these respects. An attempt was made to compare the degrees of injury by counting the sutures used but only those requiring removal were consistently recorded. For 26 index cases with the number of such sutures recorded the mean was 2·7, and for 27 controls, 3·5. This difference is not significant.

The Placenta

Comments on the placenta were usually limited to a statement of completeness, but in a number of cases other statements of abnormal appearances were recorded. Such abnormalities were recorded in 12 index cases and 3 controls, a significant difference ($\chi^2_{(1)}=5·4$, $P<0·025$). The actual comments are given in the Appendix.

The Infants

Three infants of index cases died after being

born alive and another died during labour and was stillborn. One control infant died. A difference of this degree is not statistically significant but a mortality of 4 out of 42 index cases is somewhat more than one would usually expect in a sample of this size.

None of the infants who died weighed more than 3 pounds 8 ounces. One of them, the control case, was a twin.

Birthweights were recorded regularly. The mean weight of control singletons (i.e., excluding a pair of twins weighing 2 pounds 12 ounces and 3 pounds 3 ounces) was 7 pounds 3·6 ounces and, of 42 index cases, 6 pounds 14·1 ounces. The latter of course is suspiciously low when compared with the national average and inspection of the distribution suggests that the difference can be explained upon the basis of a group of small infants in the index group. There were 7 singletons (against 3 in the controls) who weighed 5 pounds 8 ounces or less, and 4 of these 7 weighed less than 3 pounds 8 ounces. There were none below 5 pounds in the control group.

All of these very small infants died, all 4 of their mothers had severe toxaemia and 1 of them had fits, 2 had surgical inductions and another had elective Caesarean section. So it seems reasonable on prior as well as statistical grounds to infer that the mean weight of the index infants was low but that it was secondary to toxaemia and the contingent procedures whose associations with Rh-sensitization have already been demonstrated.

Sex ratios in both groups did not depart significantly from each other or from that expected in general.

Discussion

We have demonstrated associations between Rh-sensitization and the following factors: (1) Toxaemia of pregnancy as indicated by the presence of oedema and a raised diastolic blood pressure. (2) An increased incidence of surgical procedures of kinds likely to disturb the chorio-decidual junction. (3) An increased incidence of abnormalities of the placenta. (4) A possible increase in the proportion of very small infants and a raised perinatal mortality.

All of these factors are themselves intercorrelated and the fourth can be reasonably regarded as entirely secondary to various combinations of the first three. The placental abnormalities may also be regarded, in large part, as secondary to toxaemia, and some of the surgical procedures too.

In other words, if a single simple primary association is to be nominated, then it must be toxaemia. But the matter may not be so simple, for toxaemia, surgical interference, and placental disease are each in their own right likely to be associated with an increased risk of foetal-maternal transfusion and almost any interpretation of our present results, together with those of the investigations which led up to this one, must now suppose that this is indeed the important operative factor in determining sensitization to the Rhesus antigens and that once sensitization has occurred this in turn determines completely the occurrence of haemolytic disease in the next Rh-positive infant.

There is a possible objection to this conclusion and this would be through alleging that Rh or ABO blood group frequencies in toxaemic or hypertensive women differ from those in the population as a whole. With respect to the ABO groups in toxaemia such a claim has in fact been made (Pike and Dickins, 1954) but later retracted (Dickins, Richardson, Pike and Roberts, 1956), and the absence of an association confirmed by other authors (Pearson and Pinker, 1956). In any case, the original conclusion of a positive association between Group O and toxaemia is in the opposite direction to that required to explain our findings as an indirect association through maternal-foetal ABO hetero-specificity. The matter has also been put to the test in hypertension not associated with pregnancy, and, again, no association was found (Maxwell and Maxwell, 1955).

It was in order to examine a possible relationship between Rh groups and toxaemia that we assembled the secondary series of Rh-negative controls. Their diastolic pressures are given in Table IV and their obvious similarity to the paired control series, and difference from the known sensitizing pregnancies excludes a probable indirect explanation of our findings in terms of a simple blood-group association.

TABLE IV

Maximum Antenatal Diastolic Blood Pressures in 50 Rh-negative Primiparous Women

	Mm. of Mercury						Total	Mean
	–74	75–	85–	95–	105–	115–		
No. of women	5	21	21	3	0	0	50	84·4

TABLE V

Estimated Risk of Sensitization for Different Diastolic Blood Pressures

	Mm. of Mercury						Total
	–74	75–	85–	95–	105–	115–	
Sensitizing pregnancies	3	9	14	8	2	2	38
Estimated parent population	85	323	204		51		663
Estimated risk per cent	3·5	2·8	6·9	(16·0)	23·5	(→100)	5·7

We therefore reject alternative explanations of this kind. On the contrary, since haemolytic disease of the newborn is the first disease in which disturbed ABO blood group frequencies have been explained in biological terms, it is necessary rather to examine other diseases known to exhibit such phenomena to see whether they, too, are partially determined through maternal-foetal interactions.

An approximate estimate of the quantitative importance of toxaemia of pregnancy may be made in the following terms. It may be supposed that the distribution of diastolic blood pressures in the controls represents that in the population of pregnancies at risk from which the index cases are drawn, but because the risk of sensitization in this population is only about 1 in 17, the figure for the controls must be multiplied by 17 in order to represent quantitatively the parent population. This procedure supplies the necessary denominators with which to estimate the risk at different diastolic pressures. The results are given in Table V and plotted in the figure (Fig. 1). They show a steep rise in risk beginning

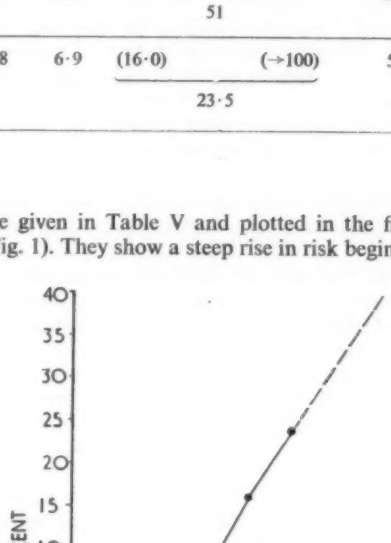

FIG. 1

Approximate risk of Rhesus sensitization according to the diastolic blood pressure.

at about 90 millimetres and a curve of increasing steepness at higher levels. The risk at lower pressures is only half of the overall risk and in this sense we can say that about half of all rhesus sensitizations are explicable in terms of this one crude factor.

Further analysis was carried out to see whether a larger proportion of cases was explicable in terms of a combination of blood pressure, obstetric procedures thought likely to promote foetal-maternal transfusion, and placental abnormalities. Using cases from both groups who had neither of these last factors and who had a blood pressure less than 85 millimetres, we computed an estimate of the risk of sensitization in such pregnancies. This came to 2·56 per cent, not much less than the figure of 2·94 per cent derived from the criterion of blood pressure alone. So far as our evidence goes we conclude that the association of obvious placental abnormalities and of surgical procedures with rhesus sensitization is largely a secondary association.

We consider that the occurrence of Rh-haemolytic disease in an Rh-positive newborn infant, depends almost always upon maternal sensitization at a previous Rh-positive pregnancy, that this dependence is complete and the consequence inevitable, and that the risk of sensitization is strongly associated with the presence of toxaemia in that pregnancy. The mechanism is probably through placental abnormalities, sometimes obvious after delivery, resulting in foetal-maternal transfusion. (The direct question as to whether the toxaemia results in the transfusion or the transfusion causes the toxaemia would be more appropriate to a study of that disease.) The association with hypertension seems, on these data, to account for one-half of all cases of rhesus sensitization, but it is possible that finer and more detailed studies of potentially sensitizing pregnancies may raise the proportion so explained. In subsequent studies, we hope to study directly the circumstances and consequences of foetal-maternal transfusion together with the effects of ABO hetero-specificity upon its frequency, the survival of foetal cells, and the risk of sensitization.

Direct studies of this kind may lead to the development of a substitute for the naturally occurring protective effect of ABO hetero-specificity, and enable one to detect and treat the women at risk before sensitization has occurred.

Summary

Previous studies have indicated the existence of an adventitious determinant of Rhesus haemolytic disease operating at the sensitizing pregnancy with a frequency of 1/17.

A series of sensitizing pregnancies have been compared with controls and differences between the groups demonstrated. The main ones are increased incidences of toxaemia of pregnancy, placental abnormalities and surgical procedures thought likely to disturb the chorio-decidual junction.

Regarding these associations as causal, it is possible thus to account for about half of all cases of Rhesus sensitization, and it seems probable that more detailed studies of abnormalities at the sensitizing pregnancies will account for still more.

Acknowledgments

The case records on which this communication is based have been put at our disposal by our obstetric colleagues, Drs. J. M. King, D. A. Smith, L. M. Snaith, F. E. Stabler and Professor J. K. Russell.

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Appendix

Stated Abnormalities of Placenta

(a) *Index Series*

Case Number	Statement
1	Soft, small, fibrotic.
2	A few old infarcts.
4	Thin, small, 5 inches diameter: fair number of white infarcts.
5	Adherent, small (manual removal).
8	Surgical induction (catheter) drew blood. Excavating clots on maternal surface. Microscopic ischaemic necrosis of villi.
11	Appears very unhealthy. Calcified (very).
13	Gross calcification.
21	Complete but unhealthy.
35	Choppy (manual removal of retained placenta).
36	Unhealthy.
39	Infarcts++.
45	Very choppy.

(b) *Control Series*

Case Number	Statement
1C	Unhealthy, necrotic, infarcted.
7C	Slightly infarcted.
43C	Edge infarcted (Caesarean section for placenta praevia).

METABOLIC STUDIES IN TOXAEMIA AND ALLIED STATES IN EARLY PREGNANCY

BY

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PRE-ECLAMPSIA and allied states form still the greatest risk to the pregnant woman. When pre-eclampsia develops in a patient at an early stage, there is an unpredictable risk if the pregnancy should be allowed to continue, especially if there is evidence of failing renal function, and the risk inherent in the method of delivery itself. A group of patients who developed eclampsia, severe pre-eclampsia or deterioration of severe hypertension has been subjected to a controlled study. Many factors may contribute to the findings in this work: the nutritional state prior to the onset of the pre-eclampsia particularly in relation to the protein intake and the proportion of carbohydrate, the period of starvation that of necessity accompanied the clinical management of the eclamptic patient, the severity of the oedema, and the need for Caesarean section to effect rapid delivery.

METHODS

Three diets were prepared of varying amounts suitable for the patient after operation and when a full intake could be resumed. Fluids taken orally or intravenously were recorded, and food refused or vomited was measured. Urine, faeces and lochia were collected in 24-hour periods, starting at 8 a.m., and blood samples were taken frequently if not daily. The haemoglobin, packed cell volume, blood urea and serum potassium and sodium were done on each sample, and daily estimations of the nitrogen, potassium and sodium excreted were made using methods described in a previous paper (Lister and Keith, 1960).

CLINICAL CASES

The 8 patients to be described fall clinically into 3 groups: 3 patients in whom the pregnancy was terminated by abdominal hysterotomy before the 28th week, 3 patients delivered by Caesarean section between the 33rd and 36th week of pregnancy, and 2 patients delivered vaginally at the 36th and 34th week of pregnancy. The need for urgent delivery in some of these severely ill patients prevented an adequate diet stabilization before delivery. In no case was lactation established.

(1) The first patient (Figs. 1 and 1a), a primigravida aged 21 years, was admitted to hospital in the 26th week of her pregnancy because of hypertension, marked generalized oedema and proteinuria, and the diet was started immediately. For more than 48 hours the strength of her convictions prevented any treatment being instituted, so that nothing could be done but observe the increase in her oedema and proteinuria. On the 3rd morning abdominal hysterotomy was performed under general anaesthesia, and thereafter rapid improvement occurred.

The second patient (Figs. 2 and 2a), a primigravida of 32 years, was admitted having had 5 eclamptic fits. Avertin controlled the eclampsia, fluids were withheld, but the oedema steadily increased until, some 10 hours after admission, hysterotomy was performed at the 26th week of pregnancy. This co-operative patient consented to live for 3 days on glucose and water, and thereafter on small additional quantities of milk as her weight was excessive. The virtual starvation may have a considerable bearing on the results.

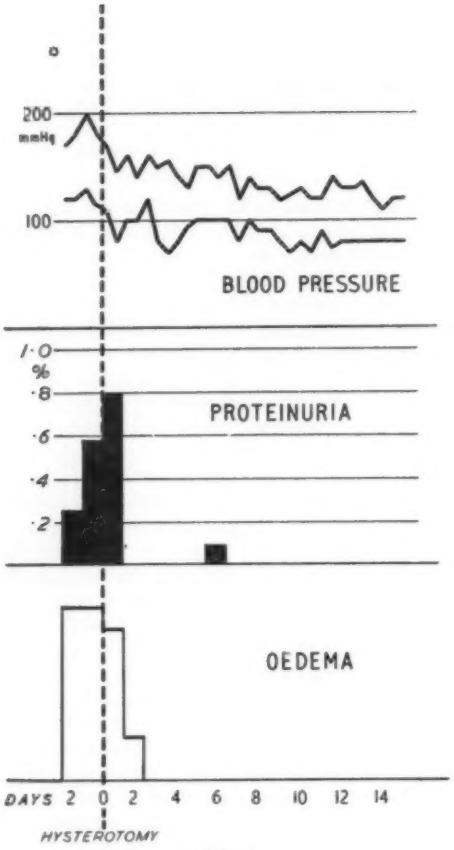

FIG. 1

Case 1. Primigravida, delivered by hysterotomy at the 26th week of pregnancy.
Chart showing blood pressure, proteinuria on the days on which it was recorded, and oedema. The oedema was generalized on the day of delivery.

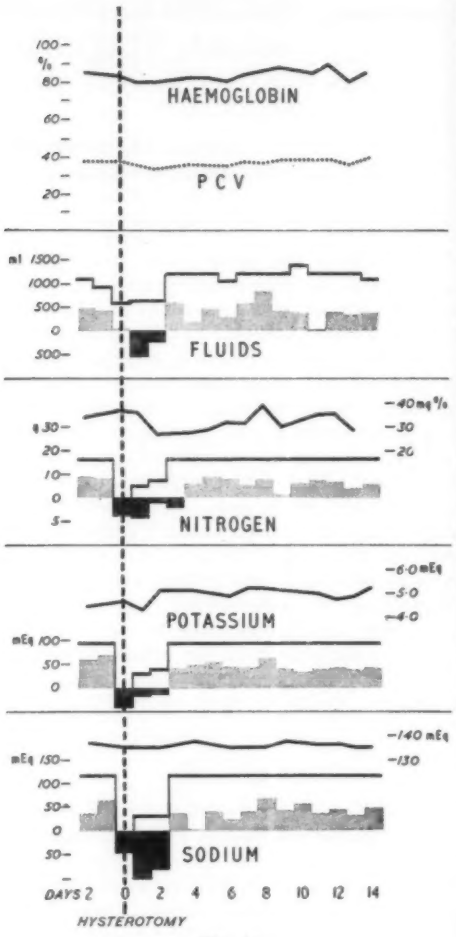

FIG. 1a

Case 1. Fluid, nitrogen, potassium and sodium balance charts. The blood urea, and serum potassium and sodium levels are shown in each section above the balance charts.

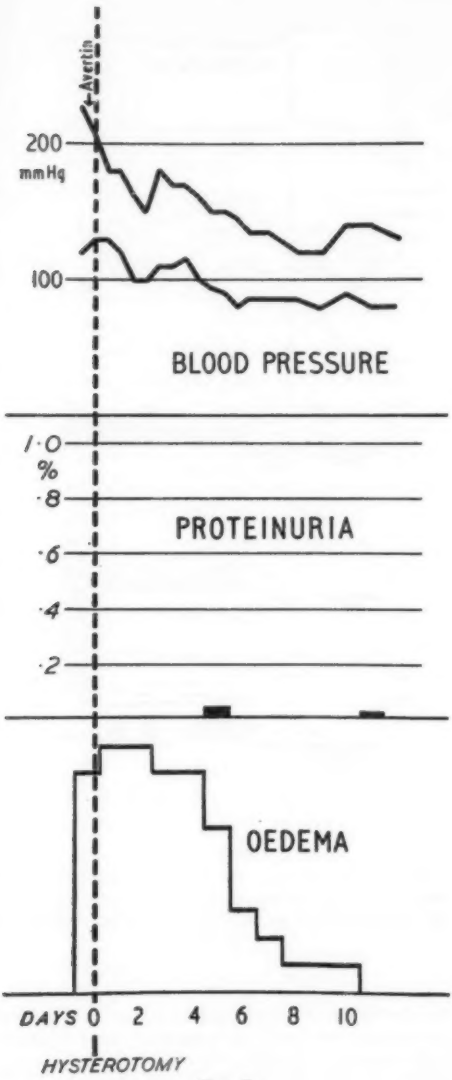

FIG. 2

Case 2. Primigravida, delivered by hysterotomy after five eclamptic fits at the 26th week of pregnancy. Avertin was given to control the fits. The urine was tested for proteinuria on only 2 occasions, and the oedema, which was gross, subsided in 10 days.

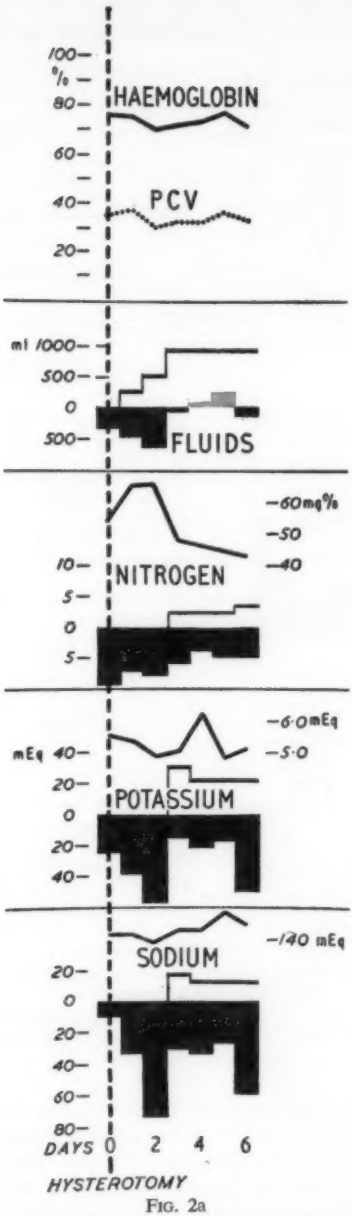

FIG. 2a

Case 2. Fluid, nitrogen, potassium and sodium balance charts. The haemoglobin, packed cell volume, blood urea and serum potassium and sodium levels are also shown.

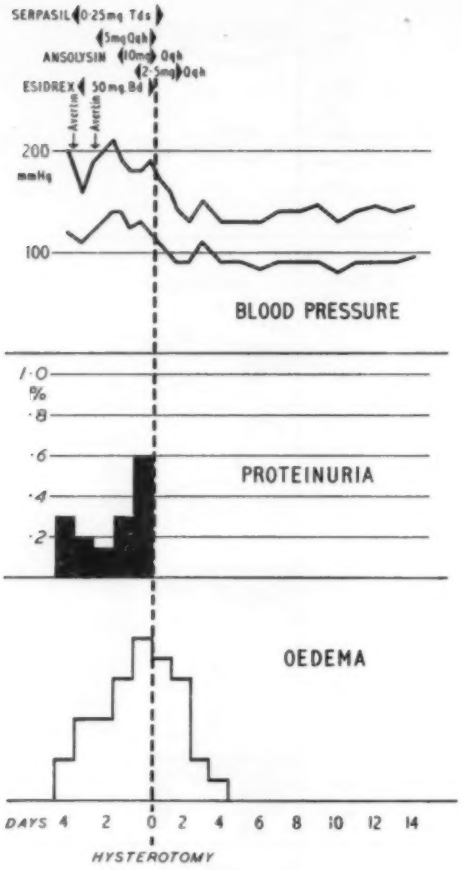

FIG. 3

Case 3. Primigravida, delivered by hysterotomy at the 24th week of pregnancy.
The blood pressure and increasing proteinuria and oedema failed to be controlled by hypotensive therapy.

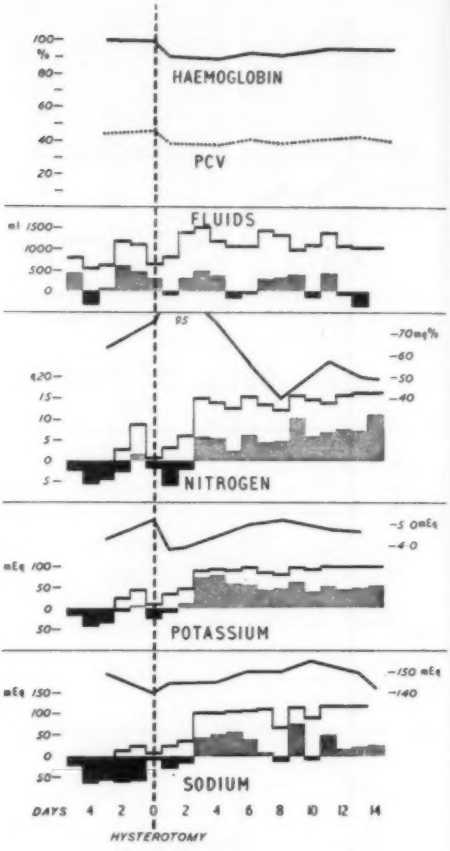

FIG. 3a

Case 3. Fluid, nitrogen, potassium and sodium balance charts. The haemoglobin, packed cell volume, blood urea and serum electrolytes are shown above the appropriate sections.

The third patient (Figs. 3 and 3a), a primigravida of 33 years, who had recently undergone a valvotomy, was admitted to hospital because of slight hypertension a few days before the onset of the test. The very rapid deterioration in signs and the development of headache were controlled to some extent by avertin which proved more effective than the increasing doses of hypotensives. It was apparent that no lasting improvement could be expected, and hysterotomy was performed at the 24th week of pregnancy under general anaesthesia.

(2) Three patients are considered together as each was delivered by Caesarean section between the 33rd and 36th week of pregnancy. The first of this group of patients (Figs. 4 and 4a) was a

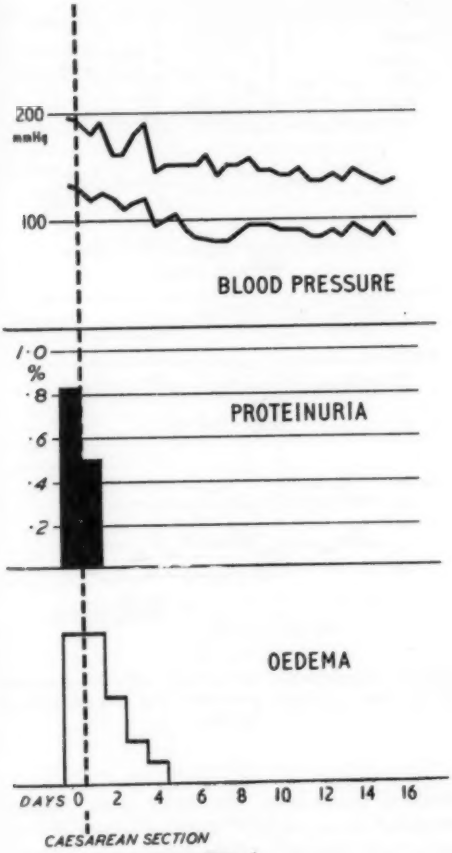

FIG. 4

Case 4. Primigravida, delivered by Caesarean section at the 33rd week of pregnancy. The oedema, which was gross, subsided rapidly after delivery. The quantity of protein in the urine was not estimated after the second day.

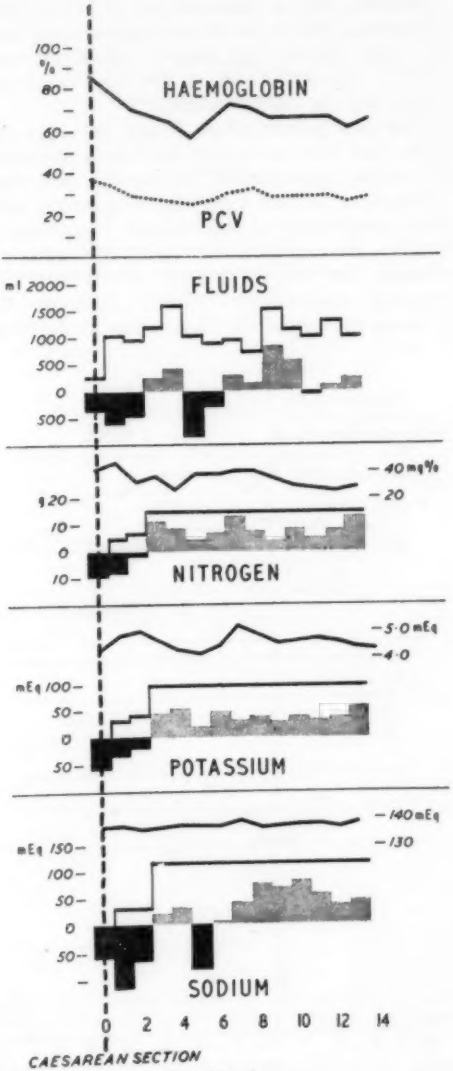

FIG. 4a

Case 4. Fluid, nitrogen and electrolyte balance charts.

primigravida of 24 years who was admitted as an emergency with a short history of severe pre-eclampsia. After a few hours observation it was felt that delivery was urgent, and Caesarean section was performed at the 33rd week of pregnancy, the child surviving.

The next patient (Figs. 5 and 5a), aged 38 years, had been in hospital for 4 weeks because of severe hypertension before the test was commenced. All her 4 previous pregnancies had been complicated by hypertension. Hypotensive therapy was supplemented with hydrochlorothiazide, but despite this the foetus was not growing satisfactorily. Within 2 hours of artificial rupture of the membranes at the 36th

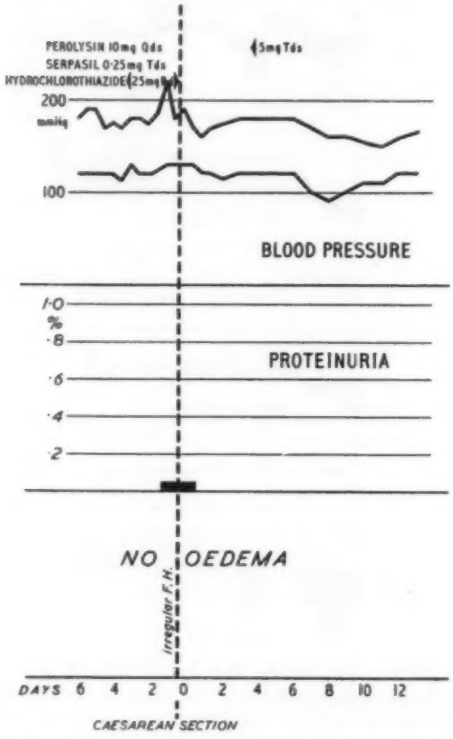

FIG. 5

Case 5. Multiparous patient, delivered by Caesarean section at the 36th week of pregnancy. Hypertension throughout pregnancy, and proteinuria immediately prior to delivery, but no oedema.

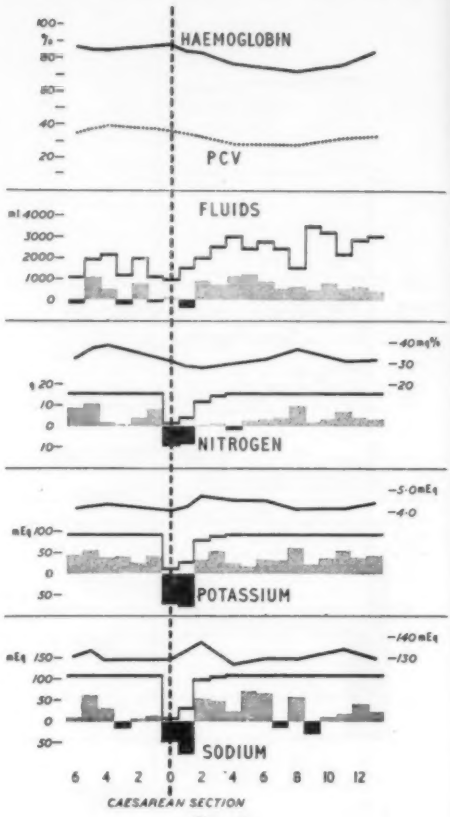

FIG. 5a

Case 5. Haemoglobin and packed cell volume estimations. Fluid, nitrogen, potassium and sodium balance charts.

week of pregnancy, the foetal heart became irregular necessitating Caesarean section for the delivery of the baby who subsequently did well.

The sixth patient (Figs. 6 and 6a), is comparable in many ways with the last. She was aged 35, her two children were 15 and 13 years old, and she had been in hospital for 3 weeks because of marked hypertension which showed slight response to hypotensive therapy. At the 35th week of pregnancy the test diet was started, but before stabilization on it could be achieved,

headache, visual symptoms and a rise in blood pressure developed and made Caesarean section essential. Though the patient improved steadily, the baby died 1 month later because of a cardiac septal defect, and the mother's fluid intake chart was also lost. The balance study was continued

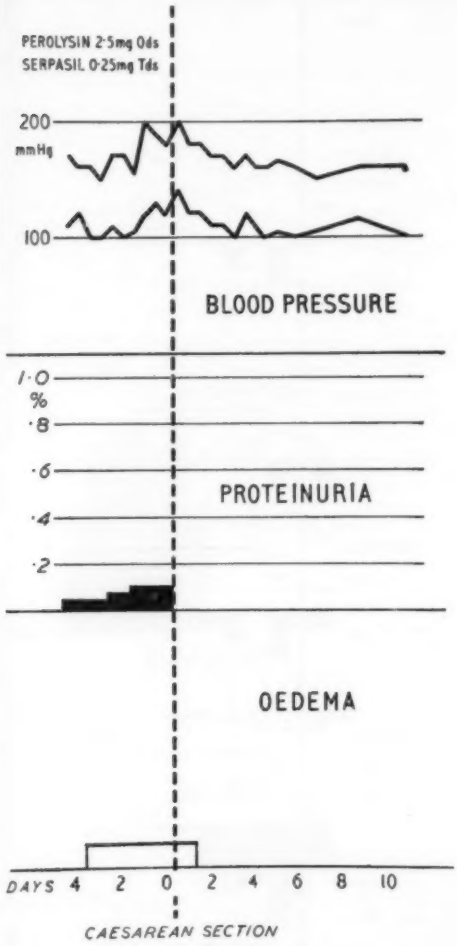

FIG. 6

Case 6. Multiparous patient, delivered at the 35th week of pregnancy, because of an exacerbation of hypertension, and the development of proteinuria and minimal oedema.

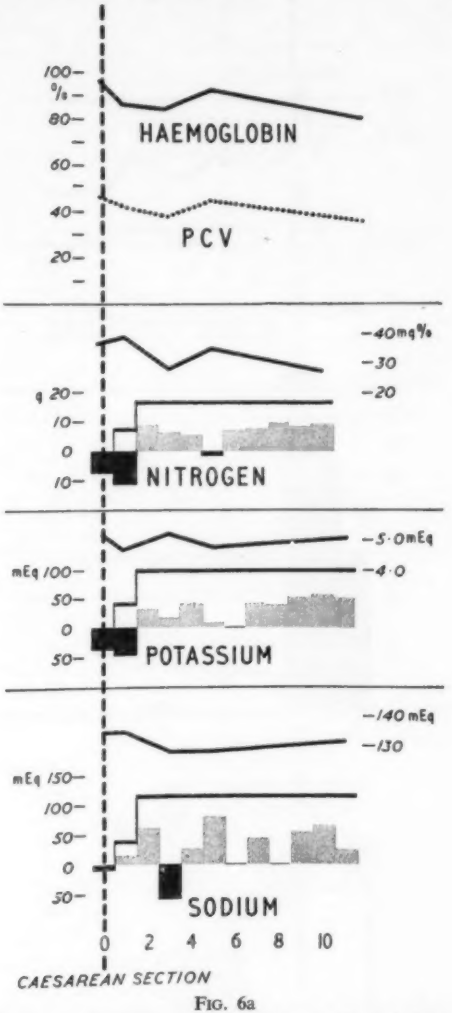

FIG. 6a

Case 6. Nitrogen, potassium and sodium balance charts. The intake for the last 2 to 3 days is inaccurate.

for 11 days after delivery, but the last 2 or 3 days must be inaccurate as the patient confessed to eating chocolate biscuits.

(3) In the last group are 2 patients who were delivered *per vaginam*. The first of these (Figs. 7 and 7a), aged 27 years, was admitted in the

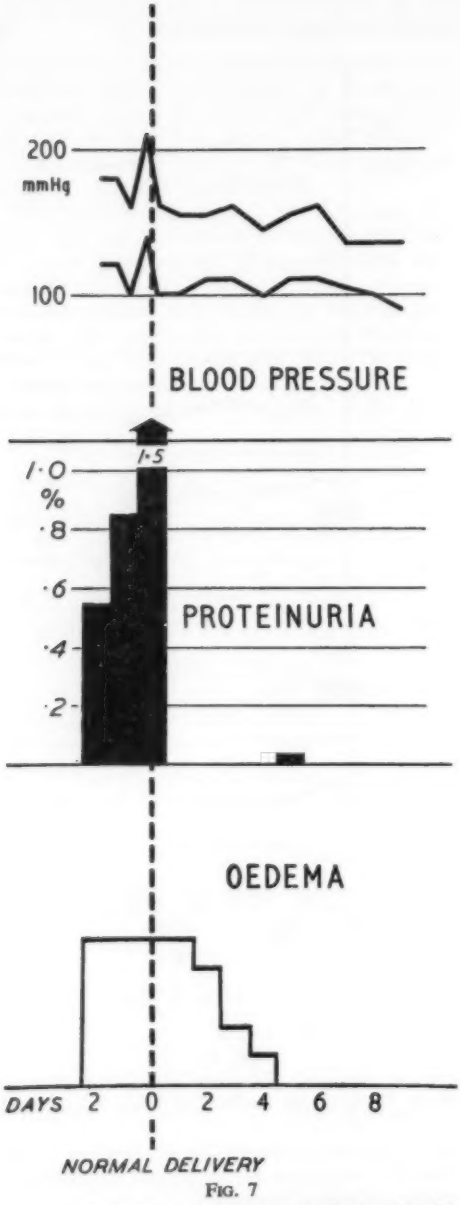

FIG. 7

Case 7. Secundipara, delivered vaginally in the 36th week of pregnancy. High levels of blood pressure and proteinuria were recorded. The oedema was generalized, but facial oedema was minimal.

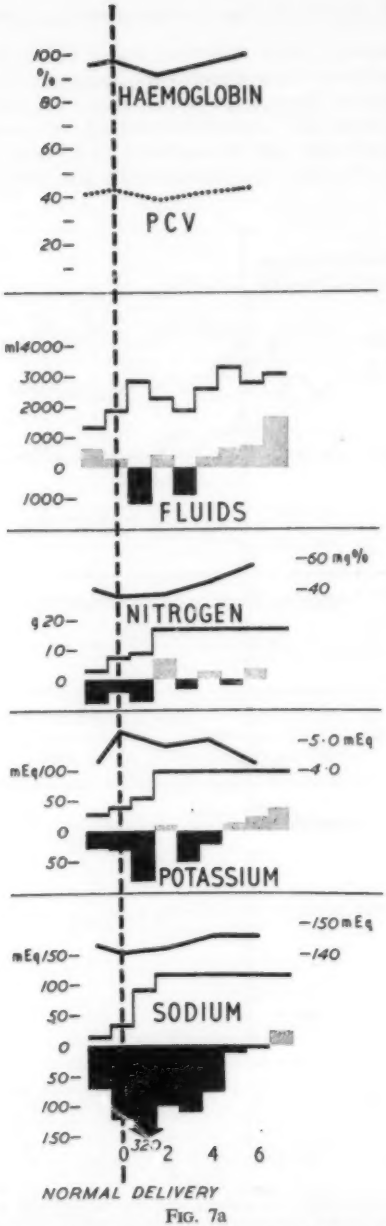

FIG. 7a

Case 7. Fluid, nitrogen and electrolyte balance charts. Note the early sodium diuresis after delivery.

36th week of her second pregnancy as an emergency because of severe pre-eclampsia, and even in the short time before delivery deterioration was apparent. The membranes were ruptured and labour soon started lasting less than 3 hours.

The last patient (Figs. 8 and 8a), a primigravida, aged 27 years, had a twin pregnancy with marked hydramnios but no oedema. After 5 days stabilization on the diet the test was commenced. Spontaneous labour started, lasted 34 hours and resulted in living twins at the 34th week of pregnancy.

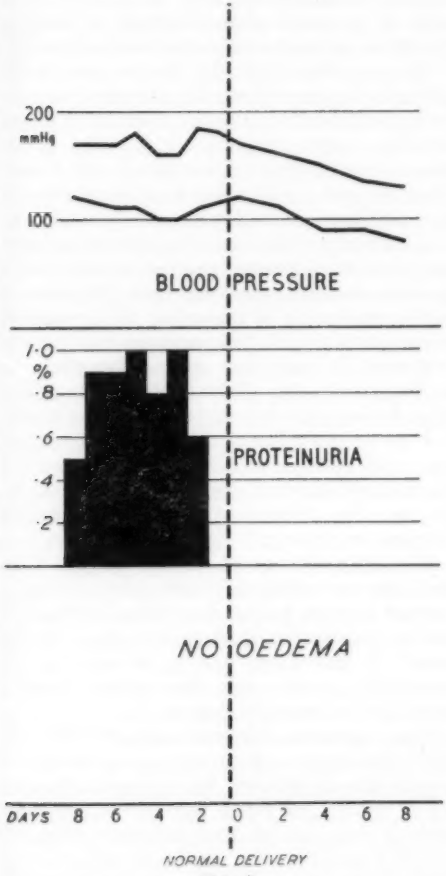

FIG. 8

Case 8. Primigravida, delivered normally at the 34th week of twins. No oedema was detected, but the proteinuria was considerable, until tests were discontinued at the onset of labour.

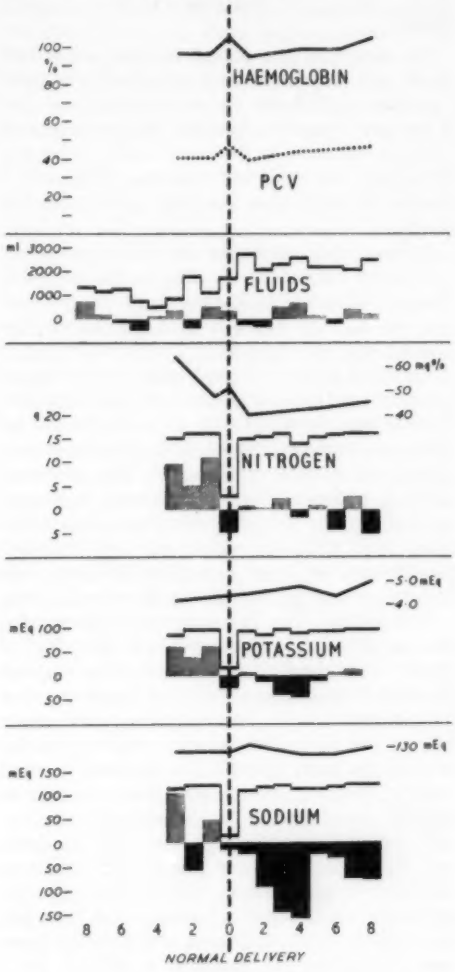

FIG. 8a

Case 8. Fluid, nitrogen, potassium and sodium balance charts.

Results

Fluids

The length of the period on controlled fluid intake and diet varied very considerably in these 8 patients, as did also the extent of the oedema. It has been assumed that the insensible loss of water is balanced by the water in the food and the water of oxidation (Bland, 1956)—these sources of water have not been included in the charts.

In those cases where the antenatal control was sufficiently long (Figs. 1a, 3a, 5a, 7a, 8a) there was retention of fluid, though in no instance was the amount great despite the increase in oedema that was marked in 1 patient (Fig. 3).

The fluid intake was inadequate on the day of operation in 2 cases (Figs. 1a, 4a), and a negative balance was shown lasting 48 to 72 hours, yet when the gross oedema of these patients is considered the diuresis seems small. The second of these 2 patients (Fig. 4a) showed a second diuresis on the 5th and 6th days, but, apart from this and the short time at delivery, equilibrium, or even a positive balance, was maintained in these patients to the end of the test.

In 1 patient (Fig. 3a), delivered abdominally, the oedema was gross, but on the day of hysterotomy the fluid intake was adequate, and the fluid balance was positive. A slight negative balance was seen the following day, again on the 5th and 6th days after delivery, and towards the end of the test. Overall she showed a small positive balance, but despite this her oedema rapidly disappeared. The hypertensive patient with no oedema (Fig. 5a) was able to drink well on the day of Caesarean section and was virtually in equilibrium. For 1 day only she showed a small negative balance, and then like the other patients delivered abdominally there was a considerable retention (9,000 ml. in 2 weeks).

Fluids were withheld from the unconscious eclamptic patient (Fig. 2a) for the 10 hours before her hysterotomy, yet the oedema clinically increased. It is necessary to consider the post-operative course of this patient separately as she received no food during the 6 days of the test. She showed a more marked initial diuresis, and was the only patient delivered abdominally with an overall negative balance.

Two patients were delivered vaginally: the first (Fig. 7a) of these was grossly oedematous, and following delivery her urinary output was considerable before she reverted to a fluid retention on the 4th day. Both the cases delivered vaginally (Figs. 7a, 8a) maintained a slight positive overall balance for the 8 and 9 days in the puerperium.

Nitrogen

The patients all appeared to be in a good state of nutrition when admitted to hospital though an accurate assessment was not possible.

Three patients (Figs. 1a, 5a, 8a) were on an adequate nitrogen intake for a number of days before delivery, and each showed nitrogen retention varying from 1·5 g. to 10·5 g. per day. A negative balance was seen in the 2 cases (Figs. 3a and 7a) as a result of the starvation only slightly augmented by increasing proteinuria.

The first 6 patients were delivered abdominally and because of the starvation associated with a general anaesthetic there was negligible nitrogen intake on the day of operation, and a negative balance was found. This negative balance was continued in each case during the phase of inadequate intake. Only in the first patient (Fig. 1a) was the balance still negative on the 3rd day despite a full diet, but at this time there was a fall in blood urea of 20 mg. per cent. All the patients delivered abdominally (Figs. 1a, 3a, 4a, 5a, 6a) showed a considerable overall nitrogen retention during the puerperium.

Case 2 must be considered separately as at no time was the nitrogen intake sufficient, and a marked negative balance was sustained throughout the puerperium. This would seem to be the result of starvation, hardly affected by the proteinuria, rather than the negative balance attributed to tissue involution.

The 2 patients delivered vaginally (Figs. 7a and 8a) both had a small nitrogen consumption on the day of delivery, but a negative balance which lasted 2 and 1 days respectively. The more severely toxaemic of these 2 patients (Fig. 7a) was in equilibrium for the whole period of the test including the day of delivery, but in the last case (Fig. 8a) there was a small overall negative balance, the more expected result in the puerperium.

The blood urea results showed in 2 cases (Figs. 1a and 3a) rising levels to the day of delivery, the rise being continued for a day after delivery in some instances (Figs. 2a, 3a, 4a, 6a). After an immediate fall, the blood urea rose again in the later puerperium except in those cases where high levels had been reached at delivery (Figs. 2a and 3a).

Potassium

The potassium charts follow the nitrogen results very closely. In cases where an adequate diet was taken before delivery a retention of potassium was seen (Figs. 1a, 5a, 8a), and, as in the nitrogen balances, 2 patients (Figs. 3a and 7a) on a small intake were in negative balance.

The day of operation showed a negative balance in each patient though it exceeded 50 mEq. in 2 cases only (Figs. 4a and 5a), and this negative balance was continued until an adequate intake was resumed in 2 or 3 days. Thereafter, there was a retention of potassium in each case, and equilibrium was not attained by the end of the test. The overall potassium balance in the puerperium was positive in these 5 operative cases (Figs. 1a, 3a, 4a, 5a, 6a).

The second patient (Fig. 2a), with negligible potassium intake, maintained a negative balance for the duration of the test.

The 2 patients delivered vaginally (Figs. 7a, 8a) present a different picture. In the first of these 2 cases there was an appreciable loss on the day after delivery, and despite some retention for the last 3 days the overall balance after delivery was negative. The initial potassium loss was less marked in the last patient (Fig. 8a) but she too was in negative balance for the 9 days of the puerperium.

There was in most cases a rise in serum potassium until the day of delivery or the day after. In the cases delivered abdominally a fall in serum levels was seen after operation, followed by a slight rise. The 2 patients delivered vaginally showed one a fall during the puerperium (Fig. 7a), and the other a rise (Fig. 8a).

Sodium

Gross oedema was present in 5 patients (Figs. 1, 2, 3, 4, 7) and it would seem reasonable that, in the 1 case (Fig. 1a) in which there was an adequate sodium intake, there should be sodium retention on the 2 days before hysterotomy. Two patients (Figs. 2a, 4a) were delivered within a few hours of admission, and 2 more (Figs. 3a, 7a) on minimal intake had large negative balances before delivery despite increasing oedema.

Three patients (Figs. 5, 6, 8) had no clinical oedema, and 2 of these patients (Figs. 5a, 8a) retained sodium on an adequate antenatal intake. No antenatal observation was made on the third case (Fig. 6a).

All the 6 operative cases sustained negative sodium balances on the day of delivery and during the days of inadequate intake, the loss being considerable in 2 of the patients with gross oedema. In 1 case (Fig. 4a) there was a second diuresis on the 5th post-partum day, but with this one exception all patients showed a retention of sodium once a normal diet had been resumed, and all were in overall positive balance during the days of the puerperium on the test (Figs. 1a, 3a, 4a, 5a, 6a). Case 2 must again be considered separately as her continued inadequate sodium intake led to a negative balance throughout.

The 2 patients delivered vaginally are in marked contrast (Figs. 7a, 8a). Case 7 with gross oedema had an immediate enormous diuresis, only on the last day of the test retaining 24 mEq., and Case 8 was in negative balance throughout the puerperium, though on no day was the loss greater than 160 mEq.

The serum sodium showed little change throughout the investigation in 4 cases (Figs. 1a, 2a, 4a, 8a). A fall in level was seen immediately after delivery in 2 patients (Figs. 6a, 7a) and in 4 (Figs. 3a, 5a, 6a, 7a) there was a rise in the later puerperium.

Discussion

The management of the patient who develops severe pre-eclamptic toxaemia at an early stage of pregnancy presents many problems. Metabolic changes have been demonstrated in normal pregnancy and the puerperium, and when pre-eclampsia complicates the pregnancy. In this paper an attempt has been made to evaluate the effect on the fluid, nitrogen and

electrolyte balance of vaginal and abdominal delivery and of starvation.

The antenatal period is associated with the retention of fluid, nitrogen and electrolytes in the normal patient (Venning, Dyrenfurth, Lowenstein and Beck, 1959; Freyberg, Reekie and Folsome, 1938). Venning and her associates found that the balance pattern varied from case to case and bore no relationship to the weight of the patient before delivery. The excretion of nitrogen, potassium and sodium fluctuated considerably post-partum with definite periods of diuresis of these various constituents which occurred simultaneously. The overall nitrogen balance was negative in the puerperium, and De Alvarez and Smith (1956), quoting Hunscher, confirm this negative balance, which reflects in his opinion, tissue involution. Venning *et al.* found a potassium balance that tended to come into equilibrium or be slightly negative, and the sodium balance remained positive for the short period of the study. Serum non-protein nitrogen, potassium and sodium levels tended to rise after delivery (Venning *et al.*), and Cadden and Farris (1938) have shown an increase in non-protein nitrogen and blood urea in labour which continued into the puerperium.

When pre-eclampsia supervenes, a retention of fluid finally results in visible oedema (Chesley, 1944; Dieckmann *et al.*, 1949; De Alvarez and Smith, 1956). Many methods have been described for the early detection of the excessive water retention, and particular attention was drawn by Hamlin (1952) to weight gain in the middle and last trimester of pregnancy. MacGillivray and Buchanan (1958) demonstrated that sodium retention in pre-eclampsia is disproportionately small in relation to water retention. Similarly there is no significant difference in total exchangeable potassium in normal late pregnancy and in cases complicated by pre-eclampsia. De Alvarez and Smith's patient in late pregnancy on a low salt intake was in negative sodium balance, a finding in contrast with the sodium retention report by many obstetricians (Dieckmann and Pottinger, 1957).

It has been seen countless times that oedema disappears after delivery, and many authors report a diuresis in the early days of the puerperium (Chesley, 1944) which is increased in the pre-eclamptic patient (Dieckmann *et al.*, 1949; De Alvarez and Smith, 1956). De Alvarez and Smith, in a study of one pre-eclamptic patient, found the nitrogen balance was negative in the puerperium, potassium was retained for 4 days after delivery, and the balance then became negative when the salt intake was increased. The serum non-protein nitrogen rose in the antenatal period, and after this rise had been sustained for a few days in the puerperium there was a significant decrease. No consistent trends were found in the serum potassium and sodium levels.

In those patients that were observed for long enough antenatally fluid retention was found (Figs. 1a, 3a, 5a, 7a, 8a), but in no case was the urinary output severely limited. Hydrochlorothiazide produced a brief negative balance, but did not alter this overall fluid retention. In the few hours before hysterotomy in the eclamptic patient there was an increase in oedema despite no fluid intake. Total body water varies in each individual, and is related mainly to the lean tissue (Bland, 1956). Fat women tolerate dehydration badly, so perhaps the retention of fluid is also badly tolerated, and certainly this eclamptic patient was obese.

In addition to fluid retention nitrogen, potassium and sodium were also retained in those cases in which the intake was adequate, but the period of antenatal study was curtailed because of the severity of the signs in these patients.

Only 2 patients were delivered vaginally (Figs. 7a and 8a) and both these patients were in overall positive fluid balance in the puerperium. The patient with marked oedema did, however, show a diuresis 48 hours after delivery, but later a fluid retention. The nitrogen and potassium balances fluctuated considerably tending to be negative, but it was in the sodium balances that a prolonged and substantial loss was seen. Blood urea levels fell after delivery, rising later in the puerperium, and the serum potassium and sodium levels differed in the 2 patients. These findings are in agreement with those of other obstetricians, though the fluid and sodium excretion require further study. It is difficult to draw any firm conclusion from 2

cases, but they serve as a comparison for the patients delivered by Caesarean section.

Following Caesarean section in the normal patient and for the next 3 to 4 days a positive fluid balance was found, tending then to be negative or in equilibrium (Lister and Keith, 1960). The day of operation, associated with no nitrogen intake, showed a negative balance which continued negative only so long as the intake was deficient, there being an overall retention of nitrogen in some cases. The potassium results followed very closely those for nitrogen, but in each case a retention was seen over the whole period of the test in the puerperium. Sodium balances differed in each patient, a negative balance on the day of Caesarean section followed by retention and a second diuresis, but in 1 case there was a strong sodium retention for 6 days followed by an almost equal loss, consistent with the picture seen after surgical operation (Moore and Ball, 1952).

When the very considerable oedema that was present in some of the patients in the present series is taken into account, the negative fluid balance following Caesarean section is surprisingly small, and yet the clinical improvement was maintained. In all the cases, except the eclamptic patient, who must be considered separately, there was an overall fluid retention for the length of the test after delivery, though perhaps a longer study might have altered this finding. The fluid retention in the patient with no clinical oedema reached 9,000 ml. in 14 days after Caesarean section.

Nitrogen utilization may be affected by the amount of carbohydrate in the diet and the previous state of nutrition of the patient, but all these patients seemed adequately nourished. The patients delivered abdominally showed a negative nitrogen balance on the day of delivery and during the short period of inadequate intake. Thereafter there was a nitrogen retention, resulting in an overall positive balance for the duration of the test after delivery. In no case was the blood loss at delivery excessive, but even if it had been taken into account the nitrogen retention would have been reduced but not rendered negative.

The potassium results resembled the nitrogen findings, and showed an overall potassium retention in the puerperium. These results are consistent with those reported earlier in non-toxaemic patients delivered by Caesarean section, and show the influence of the operation on the pregnant patient. Similarly 5 patients delivered abdominally, despite in 3 patients a second sodium diuresis, showed a retention of sodium in the puerperium. The immediate effect of Caesarean section and reduced sodium intake, was a negative balance and not the retention reported by Moore and Ball (1952) after a surgical operation during the early phase of nitrogen and potassium loss.

The blood urea, serum potassium and serum sodium levels are in general agreement with other reports in the puerperium. Comparatively high blood urea levels are recorded especially in the cases before the 28th week of pregnancy.

Starvation is associated with a negative nitrogen and potassium balance, the daily excretion being no greater than before the starvation began, but after a 2-day period of loss sodium is conserved by the kidney (Moore and Ball, 1952). The eclamptic patient, delivered by hysterotomy, showed the influence of her continued inadequate diet, and was the only patient to exhibit negative fluid, nitrogen, potassium and sodium balances after delivery. In all these except the sodium chart, where no conservation of sodium was found, the influence of her starvation predominated.

The metabolic changes in the toxaemic patient still have not been unravelled, for many factors influence the picture. Among these will be the nutrition of the patient, the relationship to each other of the various ingredients in the diet, and the ultimate fate of the fluid balance. But in arriving at the metabolic pattern, consideration must be given to the duration of starvation that may accompany the treatment of the severely ill patient, and the influence of the metabolic changes associated with operation.

I would like to thank Mr. H. Grayshon Lumby for the care he has taken with the charts.

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THE TREATMENT OF ECLAMPSIA

BY

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IN many countries the incidence of eclampsia has fallen considerably in recent years (Hamlin, 1953), but in the developing lands the disease is still an important cause of maternal death. Whilst in Western countries eclampsia is a dying disease, in the developing lands of the world it remains a killing disease. It is unfortunate that in these lands there is a great shortage of trained medical and nursing staff. This means that any treatment proposed to deal with the problem of eclampsia must make the fewest possible demands on the available staff.

AETIOLOGY OF ECLAMPSIA

Until the cause of pre-eclampsia and eclampsia is known, treatment must be largely symptomatic. Recently a theory has been put forward by Mastboom (1955) which helps to rationalize treatment. Mastboom conceives eclampsia to be due to a functional disturbance of the placental enzyme systems, caused by a diminished uterine and placental blood flow. That there is a decreased uterine blood flow has been shown by Morris *et al.* (1955). The enzyme disturbance leads to a disorder in the placental steroid metabolism producing a relatively high concentration of placental mineralo-"cortico"-steroids. These, together with a disturbance in the diuretic-antidiuretic complex, cause water (and perhaps sodium) retention and sensitize the vascular system to the pressor fraction of the posterior pituitary hormone.

MECHANISM OF THE PRODUCTION OF ECLAMPTIC FITS

There are several possibilities to account for eclamptic fits. Zangemeister (1915) postulated that they were due to cerebral oedema, but this is unlikely, as necropsy examination of the brains of women who have died in eclampsia fails to show cerebral oedema. Another suggestion is that eclampsia is a form of epilepsy invoked by the known salt and water retention. Rosenbaum and Maltby (1943) found that the presence or absence of a pre-existing cerebral dysrhythmia might be the determining factor in many patients, but James (1955) has produced contrary evidence. McCall (1953) has shown that there is a marked reduction of cerebral blood flow in pre-eclampsia and eclampsia, probably due to cerebral vascular spasm. Darrow (1945) noted, in animals, that when cerebral vascular spasm occurred there was an increased incidence of cerebral dysrhythmia. This would explain Jost's (1948) finding that cerebral dysrhythmia patterns in eclamptic women became normal as their hypertension diminished. This work suggests that the seizures in eclampsia are principally due to disturbed cerebral function due to impaired circulation in the brain.

RATIONAL OF THE TREATMENT OF ECLAMPSIA

In view of the above, any treatment of eclampsia must seek (1) to decrease the sensitivity of the patient's brain to external, and internal, stimuli, (2) to relieve the generalized vascular spasm and so permit a better flow of blood to the brain, the kidneys and the uterus, (3) to reduce the hypertension and (4) to aid in the elimination of the retained water and electrolytes.

There are several drugs available which will help to produce the desired effects, and their value is enhanced by certain general measures.

These are applicable no matter what drug is used for the specific treatment of eclampsia.

General Measures in the Treatment of Eclampsia

(1) *Medical and Nursing Care*

Ideally each eclamptic patient should have a doctor or trained nurse in constant attendance. The duties of the attendant are to detect any change in the condition of the patient presaging the recurrence of a fit; to maintain a clear airway, especially following a fit; and to note changes in pulse, temperature, blood pressure and urinary output. In many countries where eclampsia is common this ideal cannot be achieved because of the shortage of trained staff.

(2) *Maintenance of a Clear Airway*

A clear airway is of great importance as the accumulation of mucus in the posterior pharynx can lead to marked respiratory distress. Although Collins *et al.* (1953) advocate tracheotomy, in my experience this is rarely necessary, and simple suction is usually sufficient. In fact the only patient on whom a tracheotomy was performed died subsequently from virus pneumonia. Certain drugs are also available which will diminish pharyngeal secretion. Atropine gr. 1/100 may be given six-hourly, and will help in the early stages but is of less value later and has little effect in established pulmonary oedema. Recent experience with the phenothiazine drugs has shown them to be of greater value than atropine, and the latter is no longer used in Kuala Lumpur.

(3) *Prevention of Pulmonary Oedema*

The onset of pulmonary oedema may be due to a failing heart, or to increased transudation of fluid into the interstitial spaces of the lung and into the alveoli, consequent on pulmonary hypertension. The appearance of pulmonary oedema in the eclamptic patient is a sign of the gravest prognostic significance, and measures should be taken to prevent it. Eastman (1950) suggested that all eclamptic patients should be given digitalis, but to be of value this must be given before pulmonary oedema is established. When it is present, intravenous aminophylline is of greater value. Venesection has been suggested, and undoubtedly aids in treating pulmonary oedema in the non-pregnant. In pregnancy, particularly as many eclamptic patients are also anaemic, the measure may be more damaging than beneficial.

The position of the patient is important. Whilst a slight Trendelenburg position is of help in draining away retained pharyngeal mucus, the patient is more liable to develop pulmonary oedema. For this reason she should be nursed with the head slightly raised, if this is possible. Should pulmonary oedema develop, oxygen bubbled through alcohol may be of value. Two patients treated in this way showed marked improvement but in two others little effect was noted.

(4) *The Prevention of Cyanosis*

Any episode of maternal anoxia constitutes a danger to mother and baby, and continuous oxygen should be given to the eclamptic patient. In this Department the practice is to give continuous oxygen to all eclamptic patients by means of a nasal catheter, and to keep an anaesthetic machine ready beside the patient so that higher concentrations of oxygen under positive pressure may be given if needed.

(5) *The Promotion of Diuresis*

Since water and electrolyte retention is known to aggravate the symptoms of eclampsia, the elimination of both should be of value. Control of the convulsions and the reduction of renal vascular spasm are the most effective ways of promoting diuresis, although Dieckmann (1952) believed intravenous hypertonic glucose, in distilled water, to be useful. The evidence on this point is not complete for many of the patients who obtained a diuresis after the use of hypertonic glucose solutions might well have done so without it, merely because of concomitant therapy given to reduce the hypertension. If glucose is used it should be given rapidly and in solutions of high concentration as the infusion is liable to cause thrombosis at the site of the injection. A study of the urinary output of eclamptic patients receiving hyper-

tonic glucose solutions intravenously compared with women who received none showed no statistical difference. In general, an increased urinary output followed only when the blood pressure had been reduced from high levels, and when renal vascular spasm had been relieved. It is probable that in many reports which show the effectiveness of hypertonic glucose in producing diuresis the results have been due to the diminution of the hypertension rather than to the administration of the glucose solution. For this reason the use of the hypertonic glucose has been abandoned in this Unit.

It is also claimed that intravenous hypertonic glucose will protect the liver from theoretical toxins and from potential degeneration. Such a claim can only be sustained if it can be shown that a lesion "typical of eclampsia" is found in the liver of eclamptic patients. The histopathology of eclampsia has been investigated by Sheehan, but most reports of liver lesions were made at autopsy.

In an effort to obtain more information about hepatic pathology during the course of eclampsia, a series of liver biopsies was made on eclamptic patients, usually within 24 hours of admission. In addition four liver biopsies were taken from antenatal volunteers. The latter patients had been admitted to the antenatal ward and none had pre-eclampsia.

The findings are shown in Table I and the histopathological reports were made by Dr. A. T. Marsden, Consultant Pathologist to the Institute for Medical Research.

It can be seen that, as far as these patients are concerned, no lesions specific of eclampsia could be detected. Although fatty degeneration was found in the livers of most eclamptic patients, liver biopsies from the four "normal" pregnant women investigated showed evidence of fatty degeneration with equal frequency. Since the majority of patients encountered are living at a poor nutritional level, these findings may be due to nutritional deficiencies which would become more obvious in pregnancy. Focal necrosis of the liver was encountered in four eclamptic patients but only one of these died, and in Case 7 a second biopsy taken 24 hours later showed that, in that specimen, no necrosis existed. It is also of interest that in one

TABLE I

To Show the Results of Liver Biopsy in Pregnant Patients

	Registered No.	Pathology No.	No. of Fits	Outcome	Fatty Degeneration		
					Focal	Diffuse	Necrosis
Eclamptic Patients							
1	9299/53	1540	6	Lived	+	−	−
2	9595/53	1601	2	Lived	++	−	−
3	9360/53	1545	4	Lived	−	−	+
4	9656/53	1989	13	Died	+	−	+
5	1094/53	1784	1	Lived	−	+	−
6	12409/53	1976	3+	Lived	+	−	−
7(a) ..	16229/53	1838	3	Lived	+	−	++
(b) ..	Second biopsy 24 hours later				+	−	−
8	11675/53	1897	10+	Lived	−	++	++
9	12711/53	2019	2	Lived	+	−	−
10	1304/54	188/4	7	Died	+	−	−
11	11353/57	1161/1	1	Lived	−	−	−
Normal Pregnancy							
1	12635/53	2639	0	Lived	−	+	−
2	11225/53	1815	0	Lived	+	−	−
3	12763/	12763	0	Lived	+	−	−
4(a) ..	8737/53	1432	0	Lived	−	+	+
(b) ..	Repeat biopsy one month later				−	−	−

case of "normal" pregnancy, liver necrosis was detected.

These findings can only be considered preliminary and work is proceeding to clear further points. This will be the subject of a paper at a later date. These findings suggest that it is unlikely that intravenous hypertonic glucose, or calcium gluconate, has any protective value on the liver of eclamptic patients.

(6) *The Prevention of Infection*

The metabolic upset of eclampsia, together with the increased incidence of operative obstetrics required in eclamptic patients, makes puerperal infection more common. Many workers recommended the prophylactic use of penicillin to combat this. Today, however, with the emergence of antibiotic resistant bacteria, especially staphylococci, penicillin should be replaced by one of the "broad spectrum" antibiotics. Since the patient is usually comatose and unco-operative the antibiotic must be given parenterally, and in this series intramuscular penicillin was given originally but was replaced latterly by intramuscular or intravenous tetracycline.

(7) *The Use of Hypothermia*

Several eclamptic patients developed a high temperature in the absence of obvious infection. This pyrexia is a sign of irritation of the temperature-controlling mechanism in the midbrain. During the period of hyperpyrexia a considerable strain is thrown upon the heart, and the outlook is grave.

In an effort to combat this hyperpyrexia and to relieve the cardiac strain use was made, on two occasions, of rapid body cooling by means of ice-packs. The results were gratifying but nothing further can be claimed for the method in view of the few cases treated.

The Specific Treatment of Eclampsia

Through the years many drugs have been used in the treatment of eclampsia. They may be divided into (1) sedatives or cortical depressants, (2) hypotensive drugs and (3) combination of the previous two groups.

(1) Sedatives

The sedative drugs include morphine, chloral hydrate, paraldehyde, bromethol and the barbiturates. The greatest exponent of the use of sedation was Stroganoff, and in 1,399 cases he obtained a maternal mortality of 6 per cent (Stroganoff and Davidovitch, 1937). However, the use of morphine and chloral hydrate is attended by a diminished urinary output. Magnesium sulphate, which was introduced by Einar (1907) has been used since by many workers. It owes its popularity to its depressant action on the nervous system, and McCall and Sass (1956) have shown that it relieves cerebral vascular spasm and causes an increased cerebral blood flow. Against this, magnesium sulphate produces no hypotensive effect, and its use is often attended by painful abscesses.

In recent years there has been dissatisfaction with the traditional drugs and two new methods of treatment have been advocated. Dewar and Morris (1947) suggested the use of rectal bromethol, and O'Donel Browne (1950) advised continuous thiopentone. Both of these methods have been used in Kuala Lumpur.

Thiopentone by Continuous Infusion

In 1950 Browne suggested the use of thiopentone alone for the control of eclamptic fits. Thiopentone is a rapidly acting barbiturate which causes cerebral depression and hence should be an admirable drug to control eclamptic fits. Unfortunately it has been shown that it causes cerebral ischaemia and depresses cerebral oxygen metabolism when given in large doses (McCall and Sass, 1956). In Browne's regime the patient was rapidly sedated with 0·5 g. of thiopentone in 10 ml. of distilled water, and an intravenous infusion containing 3·0 g. thiopentone in 1,000 ml. of 5 per cent dextrose was set up. This was run sufficiently fast to produce good sedation. Browne considered that 1,000 ml. to 1,500 ml. of fluid was the maximum which should be given in 24 hours, and if the patient became restless whilst the infusion was running he was prepared to give additional intermittent doses of 0·1 g. thiopentone intravenously. He found that up to 10 g. of thiopentone could be given in 24 hours, and by the time of his death

had treated 26 patients. The maternal mortality was 7·6 per cent, and the foetal loss was 33 per cent. Menon (1953), using thiopentone as advocated by Browne, showed that although the recurrence of fits was reduced from 47 per cent to 9·5 per cent the maternal mortality was not reduced. He has now abandoned the method, claiming that "the constant careful attention which is the essence of this method gives a very anxious time to the doctor and I am constrained to admit that from my experience the results have not been commensurate with the stress and strain gone through" (Menon, 1955).

Results Using Thiopentone in Kuala Lumpur

In 1953–1954 thiopentone was used for the treatment of 55 eclamptic patients. Early on it was found that the fits were controlled better if a smaller continuous dose was used and this was supplemented by small amounts of intravenous thiopentone. In two years the drug was used in a variety of solutions. It was used diluted in 10 per cent and in 20 per cent dextrose, and diluted with dextran. The latter was suggested as a means of maintaining the blood volume and of preventing further interstitial hydration. However, experience showed that its use was followed by no benefit, and indeed was contra-indicated in view of the reports of the development of hypofibrinogenaemia following dextran infusions.

There was no difference in the results whatever solution was used, and as experience was gained it became clear that the continuous intravenous thiopentone infusion gave an anxious time to the attendants. Fits tended to recur with little warning, and often the patient became so restless that physical restraint was needed. In these episodes the intravenous needle became displaced, and several patients received painful thiopentone haematomata. In this series there was a high incidence of pulmonary oedema, despite Browne's experience that the incidence of this complication was reduced, and in three patients, who were sedated with thiopentone, hypertension was suddenly replaced by severe shock which required treatment with plasma substitutes and hypertensive agents.

In all, 55 patients were treated with continuous thiopentone. Of these 55 women, 45 lived and 11 died, 3 being admitted moribund; a maternal mortality rate of 19·8 per cent. Five mothers died undelivered and the foetal loss was 27 out of 55, or 49·1 per cent. (Table II.)

It was considered that 33 patients were successfully treated by continuous thiopentone and that there were 15 failures; 4 patients were treated with partial success and 3 could not be assessed as they died within one hour of admission. The recurrence of fits occurred in 11 patients, and 6 patients were restless but were further sedated before a fit could occur, a total of 30·9 per cent.

Bromethol

Because of the difficulties encountered using thiopentone, another method was sought which would be more effective. In 1947 Dewar and Morris reported on 44 patients treated with bromethol, with 3 deaths.

Bromethol produces rapid anaesthesia, and with an average dose maintains the patient in

TABLE II

To Show the Foetal Result Following the Use of Thiopentone for the Treatment of Eclampsia

	Abortion	Previable (500–999 g.)	Premature (1,000–1,999 g.)	Mature (+2,000 g.)
Live	–	–	10	18
Neonatal death	–	1	5	1
Stillbirth	1	8	3	3
Undelivered	–	–	2	3
Total	1	9	20	25

the second stage of anaesthesia for 4 to 6 hours (Macintosh and Pratt, 1940). The drug is detoxicated in the liver and excreted by the kidneys, where it has a diuretic effect (Brown *et al.*, 1950). It also produces a fall in blood pressure. Whilst all these effects are of value in the treatment of eclampsia a coincident respiratory depression occurs which may be dangerous.

A dose of 5·5 ml. bromethol dissolved in 223 ml. water is suitable for the average patient (Campbell and Burton, 1952). Before administration the mixture should be tested with Congo red to detect the presence of degradation products. Bromethol is given rectally and a second dose may be given after 3 hours, but Dewar and Morris (1947) found that more than three doses in 24 hours were seldom required.

The results of three series, compiled by Stern and Burnett (1954) showed that the maternal mortality in 149 cases was 4·03 per cent, and the foetal loss was 32·58 per cent. The incidence of recurrent fits was less than 10 per cent.

Results Using Bromethol in Kuala Lumpur

These results seemed so good that the use of thiopentone was abandoned and bromethol was used instead. In 1954–1955, 22 patients were treated: 18 mothers lived and 4 died, 2 being admitted moribund; a total maternal mortality rate of 18·2 per cent. Two mothers died undelivered, and the foetal loss was 7 out of 22 or 31·6 per cent (Table III).

There was a recurrence of fits in 9 patients (28·1 per cent). This is very much higher than that reported in other series. The method used was similar to that advocated by Dewar and Morris (1947), and, if a patient became restless in the intervals between using bromethol, small doses of 0·20 g. thiopentone were given intravenously.

Certain difficulties became apparent. The patients needed considerable care and control, and the attendants had to be alert to detect the onset of pulmonary oedema. The amount of pharyngeal mucus was a constant worry and the pharynx required frequent suction. But perhaps the greatest difficulty was in the administration of the rectal bromethol. Too often there was a return of the fluid and the quantity lost was not easy to determine. In some patients the administration of the enema was very difficult because of their great restlessness, and initial sedation of the patient with 0·25 g. of thiopentone was found to be of value. In most patients there was a fall in blood pressure following the use of bromethol, and one patient collapsed and required restorative measures.

Despite these disadvantages, the use of bromethol produced a lower maternal mortality than did thiopentone. But the unpredictable nature of the response to bromethol, and the still high maternal mortality made the search for a better method necessary.

(2) Hypotensive Drugs

It was at this time that hypotensive drugs began to be used in the treatment of eclampsia. Reference to the literature showed that three main types of drugs were being used. These were (*a*) ganglion-blocking drugs, (*b*) the veratrum viride derivatives, such as veratrone and protoveratrine, and (*c*) hydrallazine.

Each of these groups of drugs had been used with success by different workers, but each

Table III

To Show the Foetal Results Following the Use of Bromethol for the Treatment of Eclampsia

	Previable (500–999 g.)	Premature (1,000–1,999 g.)	Mature (+2,000 g.)
Live	1	5	9
Neonatal death	–	1	–
Stillbirth	1	–	3
Undelivered	–	1	1
Total	2	7	13

required further investigation before any conclusions of its value could be made.

The ganglion-blocking drugs could be excluded at once despite the report of Penny and Shackleton (1951). Since hypertension in eclampsia is principally humoral in origin the use of ganglion-blocking drugs is irrational, and is further contra-indicated as the hypotension produced by them is largely orthostatic. There have also been reports of neonatal death from intestinal paralysis following administration of the drug to the mother.

The veratrum derivatives were more applicable, particularly in view of the remarkable results of the Cincinnati workers (Garber *et al.*, 1950). In Britain they have been used, together with intramuscular magnesium sulphate, for the treatment of eclampsia by Stern and Burnett (1954). In a series of 498 patients compiled by them, the maternal mortality was 1·81 per cent, and the foetal loss was 28·46 per cent.

Despite the excellence of these compiled results the use of the veratrum derivatives is objectionable on both theoretical and practical grounds. Kistner (1954) showed that, whilst veratrone produced a constant hypotension and bradycardia in toxaemia patients, it was associated in one-third with nausea and vomiting. He also found that 32 per cent of patients receiving the drug developed severe headaches. But more serious, Kistner found that the renal blood flow was diminished following its administration. On practical grounds the use of the veratrum derivatives is objectionable, as it requires the most meticulous supervision and skilled nursing. Indeed Elliott (1959) recommends that a team of at least two is necessary to attend to each eclamptic patient.

Kistner (1954) therefore suggested the use of hydrallazine. Given intravenously this drug produces a marked hypotension and some degree of tachycardia. Assali *et al.* (1953) studied hydrallazine and found that its use was associated with an increased cerebral and renal blood flow. It would seem from this that the drug should be of great use in eclampsia. Unfortunately there are several disadvantages. Experience with the drug in the treatment of severe pre-eclampsia showed that unless given intravenously it had little hypotensive effect, and its use intravenously required as careful control as that of the veratrone derivatives (Llewellyn-Jones, 1958).

(3) The "Lytic Cocktail" of Phenothiazine Derivatives

In 1951, Laborit and Huguenard introduced chlorpromazine into therapeutics. It is a powerful anti-emetic, has an anti-shock effect, and produces hypothermia. Combined with other phenothiazine derivatives it has been used in anaesthesia, and since 1955 there have been several reports of cases of eclampsia treated with the phenothiazine derivatives. The largest series reported to date is that of Sheares (1957). In 124 cases, he obtained a maternal mortality of 8·06 per cent, and a foetal loss of 26·2 per cent.

In order to obtain another series of patients of similar race and background to those reported by Sheares, it was determined to use the regime suggested by him with only slight modification except for one important point. Whilst Sheares performed Caesarean section frequently as a means of effecting delivery, it was decided to use more conservative methods in Kuala Lumpur.

The three drugs used are chlorpromazine, promethazine and pethidine. In combination these three produce (1) prolonged and profound sedation, (2) a fall in blood pressure, (3) a fall in body temperature, (4) some degree of protection against shock by virtue of the anti-adrenaline effect of chlorpromazine and the anti-histamine effect of promethazine and (5) drying of the pharyngeal and laryngeal secretions. The drugs should, therefore, be of value in the treatment of eclampsia.

Method of Administration

As soon as an eclamptic patient was admitted she was given 0·20 g.–0·40 g. thiopentone intravenously. This was sufficient to sedate her whilst a clinical examination was made, and the first solution of the phenothiazine derivatives was prepared. To 250 ml. of 10 per cent dextrose, chlorpromazine hydrochloride 50 mg., promethazine 50 mg., and pethidine hydrochloride

50 mg. were added (Solution I). One hundred and twenty-five ml. of this solution was run intravenously with the screw control wide open, and the remainder of the mixture was run at 200 drops a minute. The time taken to give the whole solution was about ten minutes.

Whilst the infusion was running the patient was examined vaginally and an indwelling catheter was inserted into the bladder. A decision regarding the obstetrical management of the case was made at the time of the vaginal examination.

A second mixture of the phenothiazine derivatives was also prepared. Chlorpromazine 100 mg. and pethidine 50 mg. were added to 250 ml. of 10 per cent dextrose (Solution II) and this was run, as soon as Solution I was finished, at a rate of 40 drops a minute. Further sedation was continued with intramuscular injections of chlorpromazine 100 mg. and pethidine 50 mg. given four- to six-hourly, the first injection being given two to four hours after the completion of the intravenous infusions. If the patient became excessively restless a further 250 ml. of Solution II was given, or intermittent doses of 0·1 to 0·2 g. of thiopentone were given intravenously. A particularly dangerous time was at the end of the first stage of labour and as the presenting part reached the perineum.

Despite the use of these measures fits recurred in some patients but were always controlled with injections of thiopentone. Only two patients developed pulmonary oedema, and little trouble was experienced from pharyngeal mucus. The absence of these complications enabled the patients to be nursed with their head and shoulders raised: a considerable advantage in the prevention of pulmonary oedema.

Obstetrical Management

If the patient was not in labour, and provided the cervix was "ripe" and no contra-indication to vaginal delivery existed, the amniotic sac was ruptured and the onset of labour awaited, a dilute oxytocin drip being used in many cases. It was only when the cervix was found to be "pinpoint", and hard in texture that Caesarean section was performed. This is contrary to the experience of Hudson and Seah (1956) and of Sheares (1957) who performed Caesarean section much more readily. In the present series Caesarean section was performed 20 times, an incidence of 13·3 per cent. Of these Caesarean sections, 12 were performed on account of contracted pelvis, and 4 others during labour on account of marked foetal distress.

When there was maternal distress, or if any other indication arose in the second stage, forceps were used. To obtain analgesia 1 per cent lignocaine was used to effect pudendal nerve block, or else small additions of thiopentone were given intravenously. In many cases forceps were used prophylactically.

In addition to the use of the phenothiazine derivatives the general measures previously outlined were employed, oxygen and antibiotics being given to all patients, and digoxin used when necessary.

Results Following the Use of the "Phenothiazine Derivatives"

Since the introduction of this regime of treatment in 1956, 150 patients have been treated and 10 patients have died, 2 patients being admitted moribund; a maternal mortality rate of 6·6 per cent. The foetal mortality rate was 38·8 per cent.

Table IV

To Show the Foetal Results Following the Use of the Phenothiazine Derivatives for the Treatment of Eclampsia

	Abortion (0–500 g.)	Previable (500–999 g.)	Premature (1,000–1,999 g.)	Mature (+2,000 g.)
Live	–	–	22	71
Neonatal death	–	1	15	6
Stillbirth	–	7	18	9
Abortion	3	–	—	—
Total	3	8	55	86

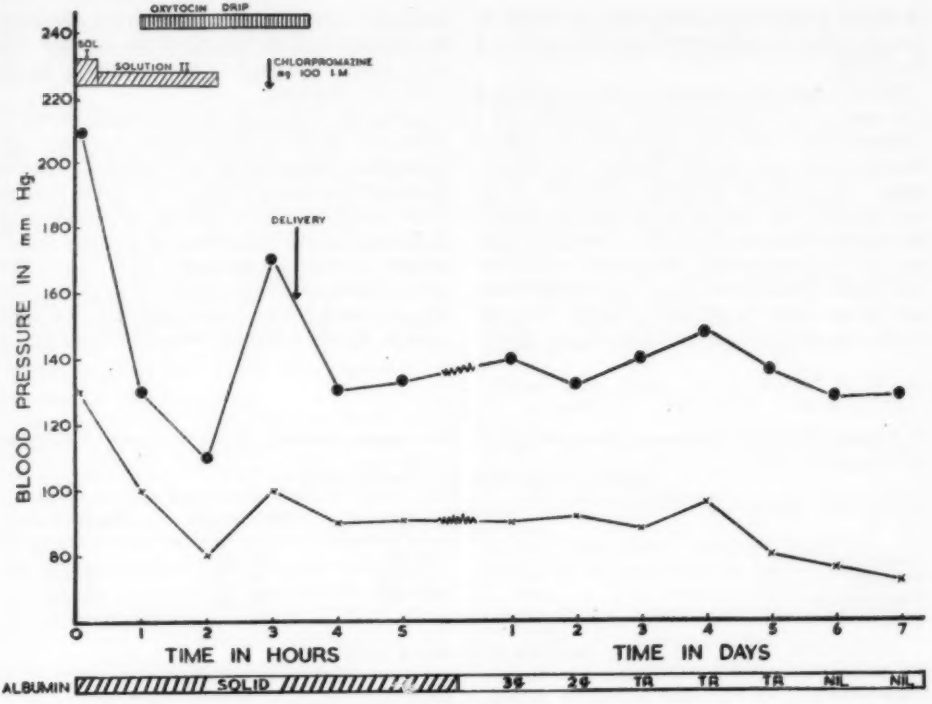

FIG. 1

To show the effect of the phenothiazine derivatives in the treatment of eclampsia. The patient was Chinese, aged 28, primigravid, and was 37-weeks pregnant. (•—• = systolic blood pressure, x—x = diastolic blood pressure.)

Sufficient experience using the drugs has now been obtained to assess their value. The most important finding has been the invariable reduction of the hypertension, and the profound sedation produced by the intravenous mixtures. Although restlessness, and even fits have tended to recur, quick and easy control has been possible by the use of additional doses of thiopentone 0·2 g. The incidence of recurrence of fits was 22 per cent.

In addition to the statistical finding of a much lowered maternal mortality rate in a homogeneous population when compared with the other drugs used, the most significant finding has been the ease of nursing obtained. This factor is difficult to analyze but the nursing sisters affirm that of the three regimes introduced since 1953 the "phenothiazine derivatives" produced a deeper sedation, less anxiety over pharyngeal mucus, less incidence of hyperpyrexia and less evidence of "toxicity". A typical case is shown in Figure 1.

DISCUSSION

This paper is the result of a study of all the cases of eclampsia admitted to a single hospital between 1953 and 1959. During this time a total of 227 eclamptic patients were treated and the number of admissions was 50,000. The incidence of eclampsia was 0·45 per cent.

As the incidence of eclampsia is decreasing in most countries the majority of workers find difficulty in obtaining a sufficiently large series

on which to report and fewer still are liable to compare different methods which they have used personally.

The fact that these patients have been treated by a team of doctors and nurses under the same direction, and that the conditions of life in Malaya have not altered during the period, makes comparison possible, although it is realized that the validity of the results cannot be as great as in a random trial. Despite this the use of "phenothiazine derivatives" together with small intermittent doses of thiopentone, have been shown to produce a lower maternal death rate than any other method previously used, and to be associated with a lesser morbidity and greater ease of nursing of the patients. The latter has been remarked upon especially by the senior nursing staff.

A further purpose of this investigation was to determine whether the lowered mortality rate using the "phenothiazine derivatives" was due to an increased use of Caesarean section to effect delivery. If comparison with the results obtained in Singapore is valid, where in a series of 124 patients a maternal mortality of 8·04 per cent and a Caesarean section rate of 27·4 per cent was obtained, the maternal mortality of 6·6 per cent in Kuala Lumpur, with 150 cases and a

TABLE V

To Compare the Use of Thiopentone, Bromethol and the Phenothiazine Derivatives in the Treatment of Eclampsia

Incidence of Fits (Maternal deaths in brackets)

	Ante-partum	Intra-partum	Post-partum
Thiopentone	35 (6)	13 (3)	7 (2)
Bromethol	8 (2)	9 (1)	5 (1)
"Phenothiazine"	72 (7)	58 (3)	20 (0)

Incidence of Caesarean Section

Thiopentone	3 patients out of 55
Bromethol	2 patients out of 22
"Phenothiazine"	20 patients out of 150

Maternal and Foetal Mortality

	Number	Maternal Mortality		Foetal Loss*	
		No.	%	No.	%
Thiopentone	55	11	19·8	27/55	49·1
Bromethol	22	4	18·2	7/22	31·6
"Phenothiazine"	150	10	6·6	59/152	38·8

Percentage of Babies in Each Weight Group

	Thiopentone	Bromethol	Phenothiazine
Abortion (less than 500 g.)	1·8	0·0	1·9
Previable (500–999 g.)	16·3	9·1	5·3
Premature (1,000–1,999 g.)	35·4	31·8	36·2
Mature (2,000 g. or more)	45·5	59·1	56·6
	100·0	100·0	100·0

* Including abortions.

section rate of 13·3 per cent, indicates that it is the use of the "phenothiazine derivatives" which is the important factor in reducing the mortality.

In Table V the three methods used in Kuala Lumpur are compared.

The treatment of eclampsia must be considered (1) in the patient's home, (2) during her transport to hospital and (3) in hospital.

For the *immediate control of the convulsions* there is no doubt that intravenous thiopentone is the most useful drug. This may be followed by rectal bromethol to sedate the patient *during her journey to hospital.* Alternatively, the "phenothiazine derivatives" given intravenously may be used for this purpose.

In hospital the "phenothiazine derivatives", together with small doses of thiopentone, used as outlined in this paper, gave the lowest maternal mortality of all the methods used in the survey. In addition the use of these drugs proved to give the least anxiety to the nursing staff. All the patients reported in this paper were nursed in an open labour ward, where other deliveries were taking place.

Summary

The treatment of 227 eclamptic patients is reviewed. All the patients were from the same geographical area, all had comparable nutritional backgrounds and all were treated in one unit. Three methods of therapy were used. These were (1) continuous intravenous thiopentone, (2) rectal bromethol and (3) a modification of the use of the "phenothiazine derivatives", together with intermittent thiopentone.

The last was shown to be the best method of treatment being easy to administer, safe to use, and productive of the lowest maternal and foetal mortality.

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CAUSES OF MATERNAL DEATH AMONG AFRICANS IN KAMPALA, UGANDA

BY

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INTRODUCTION

MATERNAL mortality in England and Wales has been a subject of great interest for many years. This paper is an attempt to find out the causes of maternal death in a backward community in East Africa, where the problems are different.

The deaths all occurred in the Maternity Department of Mulago Hospital, Kampala, Uganda, which is attached to the Medical School of Makerere University College. The mothers coming into the Hospital are all African, mostly of Nilotic or Bantu origin. They live in or around Kampala, a town of some 40,000 inhabitants, situated at 4,000 feet almost on the Equator. Their houses are simple—one or two rooms with little in the way of drainage or water laid on. Some come from more rural areas up to a radius of 50 miles.

Patients may attend the antenatal clinics once, or more regularly, but do not always take the advice given. They do not entirely trust the doctors at the clinics and generally refuse admission unless they feel ill. If any pressure is brought to bear, they may disappear entirely. The Baganda (the largest local tribe) are great believers in charms and native medicines, especially those that have to be taken during pregnancy to ensure an easy birth. The women avoid eating eggs, chicken or mutton as it may cause sterility. All this can be put down as "avoidable" factors, but a great deal of patience and careful education are needed in order that such superstition shall be overcome. Once in labour, transport difficulties over rough untarred roads often seriously delay the patient's arrival at hospital.

In the hospital, itself, there are still problems. The midwives are mostly young girls of simple education, with little English, and do not reach the equivalent of a State Certified Midwife in the United Kingdom. They find such things as accurate timing, counting the foetal heart and so on, difficult. Another factor that can hardly be imagined in England today is the shortage of blood and the reluctance of relatives and donors to give it. The Red Cross Society do noble work in trying to break down superstition here also.

In some ways, the obstetrical emergency cases—of which there are many—are like those that must have been seen at the beginning of the century at home; the facilities for treatment, however, are very different. Antibiotics and other valuable drugs are available and in reasonable quantities.

In the years reported on from January, 1952 to June, 1959, there were 17,519 deliveries connected with the hospital and 240 deaths, including abortions—a mortality rate of 13·7 per 1,000 births.

Arranged in clinical groups, but not according

to International Classification, the commonest causes of "true" maternal deaths were:

			Per cent of the Total
A. Deaths due to ruptured uterus	65	=	34
B. Deaths due to haemorrhage (all causes) ..	48	=	25
C. Deaths due mainly to exhaustion and shock	36	=	19
D. Deaths due mainly to sepsis and peritonitis ..	23	=	12
E. Deaths due to toxaemia and eclampsia	15	=	8

This is compared with the series in the *Report on Confidential Enquiries into Maternal Deaths in England and Wales—1952–1954* (Walker *et al.*, 1957) where the main causes of death were:

	Per cent of the Total
Deaths due to toxaemia (including toxaemic accidental haemorrhage)	22
Deaths due to haemorrhage (excluding toxaemic accidental haemorrhage)	17
Deaths due to abortion	14
Deaths due to pulmonary embolism ..	13
Deaths due to sepsis	3·8

Turning to the "Associated Deaths", of which there were 49, anaemia accounted for the greatest number, being 17 per cent of the total. Cardiac disease, the outstanding cause of Associated Deaths in England and Wales, only occurred 5 times (10·2 per cent). Pneumococcal meningitis and cerebral malaria accounted for 11 deaths.

It was unfortunate that in only one-third of the patients who died was a post-mortem performed. Permission is always asked of the relatives but frequently refused, so the diagnosis could only be surmised in some cases.

A.—Ruptured Uterus

During the time reported on there were 181 cases of ruptured uterus admitted and 65 died —an overall mortality of 36 per cent. Of these 44 (67·7 per cent) were spontaneous rupture, 11 (16·9 per cent) traumatic rupture and 10 (15·4 per cent) ruptured Caesarean section scars.

The spontaneous cases of ruptured uterus are one of the greatest problems here. The majority occur in multiparous women who have had several normal labours previously, and it is most difficult to predict which cases may subsequently rupture. The average local (Bantu) pelvis is both small and shallow with an average true conjugate of 9·97 cm. (Sibthorpe and Allbrook, 1958), compared with one of 11·83 cm. in London women, so no doubt disproportion is the main cause, together with the fact that the infants tend to become larger with each pregnancy. The average full-term infant weighs 6 pounds 12 ounces (3·06 kg.). The patients take native herbs both before and during labour, which have been proved to have a definite oxytocic action. The African uterus, if left alone, contracts very strongly—inertia and weak pains are not often seen. Practically every case came in already ruptured, many actually dying.

The traumatic ruptures all occurred early in the period reviewed and 10 out of 11 followed internal version for transverse lie, which has proved itself to be a most dangerous obstetrical manœuvre and to be avoided except in the rare case such as a second twin. There is no doubt clinically that the African uterus ruptures much more easily than that of the European.

The ruptured Caesarean section scar is perhaps the most difficult to diagnose, as it is often very silent at first. Every patient with a history of previous Caesarean section for whatever cause is urged to come into hospital for delivery. Unfortunately, many mothers wait at home deliberately, so hoping to avoid any possibility of a second operation. Of the 10 fatal cases, 9 were ruptured lower segment scars and 1 a classical scar. No doubt more cases could have lived had blood been available.

TABLE I

Distribution of Parity Among Deaths Due to Ruptured Uterus

Parity*	Number	%
1	4	6·2
2	13	20·0
3	20	30·8
4	14	21·5
5	4	6·2
6	4	6·1
7	5	7·7
8	1	1·5
Over 8	—	—
All parities	65	100·0

* Approximate throughout the Report, as patients do not always know the number of pregnancies they have had.

TABLE II

Approximate Age Distribution Among Deaths Due to Ruptured Uterus

Age	Number	%
Under 20	6	9·2
20–24	22	33·9
25–29	24	36·9
30–34	9	13·8
35–39	4	6·2
40 and over	—	—
Total	65	100·0

B.—HAEMORRHAGE

Deaths due to haemorrhage were the second largest group, and can be sub-divided as follows:

		Per cent
(1) Deaths due to abortion ..	6 =	12·5
(2) Deaths due to placenta praevia	8 =	16·7
(3) Deaths due to accidental haemorrhage (non-toxic) ..	1 =	2·1
(4) Deaths due to post-partum haemorrhage (delivered in hospital)	13 =	27·1
(5) Deaths due to post-partum haemorrhage with or without retained placenta, born at home or in a maternity centre, i.e., B.B.A.	20 =	41·6
	48 =	100·0

In all these cases the fact of having little or no blood available obviously made the mortality rate much higher than it should have been.

(1) *Abortion.* There were a large number of abortions admitted, 3,046 in all, but very few were by criminal intervention. All pregnancies are wanted here and there is no social stigma on illegitimacy. This may account for the relatively low mortality rate. It is, of course, very difficult to tell exactly why patients abort in this country. Possibly the high incidence of malaria, giving repeated attacks of fever in early pregnancy, may have something to do with it. Very frequent intercourse also may be another reason. Syphilis is common but probably only causes abortion round about 20–26 weeks. The Kahn test is practically never positive in patients who abort before 12-weeks gestation. Whether the severe protein deficiency in some of the mothers, or the fact that so many of the men have chronic venereal disease, causes lowered fertility and subsequent miscarriage, is not really known.

(2) *Placenta Praevia.* This accounted for 8 deaths, one being in a primigravida and the rest in multigravidae. It is interesting to note that 4 out of 8, i.e., 50 per cent, had some antenatal care. Three of the patients were delivered by Caesarean section, the others were admitted practically moribund, and, no blood being available, could not be resuscitated enough to stand operation.

(3) One case only was due to accidental haemorrhage, not associated with toxaemia.

(4) and (5) *Post-partum Haemorrhage.* There were 33 cases altogether, 13 occurring in patients delivered in hospital and 20 in patients delivered at home and brought into hospital with or without a retained placenta. These patients are some of the most pathetic cases we see. From the Table it will be noted that they were, in the main, young girls having their first babies—only one had any antenatal care. The babies were delivered at home in the village, and the placenta failed to separate in most of them. No doubt all the village women, knowing something was wrong, pushed on the fundus or pulled the cord, until at last the terrified girl was brought to hospital in a state of profound

shock. By the time she has arrived the bleeding has always stopped and the blood pressure usually unrecordable. Haemorrhage in a village, from whatever cause, must be very alarming. The patient is often far from a road, with no telephone or means of transport. The nearest cotton ginnery owner, who may possess a lorry, has to be wakened and an unwilling driver pressed into service to bring the patient to hospital. Tales are told of many dying before they reach us. On admission, resuscitation and blood transfusion was given, when available, before a manual removal of the placenta was attempted.

The deaths actually occurring in Mulago were mostly in abnormal deliveries. In 8 out of the 13 cases, the haemorrhage was associated with Caesarean section. In some of these, the patient had massive adhesions in her abdomen from previous sections, making the operation very difficult, but no doubt there were other associated factors as well. In only 4 cases was post-partum haemorrhage a cause of death following normal delivery. The average African mother loses only a small amount of blood in the 3rd stage, probably because the uterus contracts so well. One patient died of secondary post-partum haemorrhage on the eighth day.

C., D.—Exhaustion, Shock and Sepsis

There were 59 deaths altogether under this heading. Working in a backward community such as here, there are naturally a large number of deaths that can be put into this group. It is often very difficult to say exactly what was the cause of death, as it may be a mixture of all three.

There were 36 cases (19 per cent) in which exhaustion and shock appeared to be the main cause and 23 cases (12 per cent) where sepsis or peritonitis was the dominant factor.

The patients who died of exhaustion were mostly primigravidae and under the age of 25; only one had any antenatal care. These girls usually gave a history of a long labour at home and were finally brought into hospital with the foetal heart absent and the mother showing severe maternal distress. They had often been given native herbs and stories are told how some are beaten or tied up to trees to "assist" delivery. Some had a high temperature and foul vaginal discharge, and were obviously very infected. The majority were unable to deliver themselves because of disproportion associated with occipito-posterior or deep transverse arrest of the head. Uterine contractions had usually stopped and often the caput was visible at the vulva, although, owing to the shallow pelvis the main mass of the head could be felt above the brim. After resuscitation, many patients could be delivered by perforation of the head and extraction with forceps without rotation. It was not necessarily a difficult procedure. No crushing instruments were ever used. Death usually occurred a few hours after delivery, or sometimes during efforts to get the patient fit to stand an anaesthetic. When the foetus had

Table III

Age Distribution Among Deaths Due to Haemorrhage

Age	Abortion		Placenta Praevia		A.P.H.		P.P.H. (Hospital)		P.P.H. (B.B.A.)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Under 20 ..	1	16·7	1	12·5	–	—	1	7·7	10	50·0
20–24 ..	1	16·7	3	37·5	–	—	3	23·0	3	15·0
25–29 ..	4	66·6	2	25·0	1	100·0	5	38·5	5	25·0
30–34 ..	–	—	2	25·0	–	—	4	30·8	2	10·0
35–39 ..	–	—	–	—	–	—	–	—	–	—
40 and over	–	—	–	—	–	—	–	—	–	—
Total ..	6	100·0	8	100·0	1	100·0	13	100·0	20	100·0

been delivered it was quite common to find a fistula between the vagina and the bladder, no doubt due to the pressure of the head on the soft parts.

In the group where sepsis was the dominant feature, some already had peritonitis on admission. These patients were usually multigravidae and in 7 cases the child had been born outside the hospital and the mother came in already grossly infected.

In 9 cases the deaths were associated with delivery by Caesarean section. This may sometimes be "avoidable", as in one elderly primigravida where there was a prolapse of the cord. The surgeon, in an effort to save the infant, probably agitated the African theatre staff so much that they failed to boil the instruments properly. In other cases, however, the patient was already infected but the foetal heart present and the head well above the brim. In a few there was a possibility that the uterus was ruptured, making laparotomy essential.

Every effort is, of course, made to prevent sepsis when delivering patients in the hospital, but the majority of African nurses do not really understand the principles of asepsis; they do what they are taught when being supervised, but standards lapse when no one of authority is present. Masks are supposed to be worn for delivery but are sometimes kept in a pocket with a handkerchief! Receptacles containing antiseptic solutions, in which to drop them after use, are much in evidence but not always used.

Owing to the growing popularity of hospital confinements, there is much overcrowding, and patients are often delivered on the floor, all labour ward beds being occupied.

TABLE IV

Deaths from Sepsis Classified According to Antenatal Care or Otherwise

	Sepsis and Peritonitis		Exhaustion and Shock	
	No.	%	No.	%
None	20	87·0	35	97·2
Some	3	13·0	1	2·8
Total ..	23	100·0	36	100·0

Antibiotics, fortunately, are in good supply and, no doubt, prevent many deaths, but they are apt to be used indiscriminately by some housemen and nurses.

E.—Pre-eclamptic Toxaemia and Eclampsia

This condition, the main cause of maternal death in England and Wales, only accounted for 15—8 per cent of deaths here.

Eclampsia is not common in this part of Africa—there were only 34 cases in the time under review, some quite mild with only one or two fits during labour or immediately following delivery.

The patients with pre-eclamptic toxaemia may in some instances have had toxaemic symptoms superimposed on chronic nephritis or essential hypertension; coming in late in pregnancy it was not easy to tell, especially when a post-mortem was refused.

After 1955, a routine practice was made of testing all urine and taking the blood pressure at every visit to the clinic, although the nurses found this rather difficult to do accurately. The typical case of slowly increasing toxaemia, as seen in the European patient, is very rare here. In the African mothers, severe symptoms come on very rapidly with a sudden sharp rise in blood pressure—going quickly down after delivery.

More than half of the women with toxaemia had no antenatal care at all and even the booked cases may only have attended once or twice before admission.

There did not seem to be any seasonal variation, which is not surprising as the average temperature all the year round is 62° F. to 84° F. during the 24 hours. It is rather hotter and drier in January and February and cooler and wetter in June and July, but probably not enough to make any appreciable difference. The usual diet of the patients consists of matoke (green bananas—peeled and boiled), sweet potatoes, cassava and ground nuts, together with papaya, pineapple and certain other fruits, and plenty of salt. Around the town they eat bread, and a few more wealthy ones drink milk. Tea with a lot of sugar is the most popular drink. The patients do not come from one social class.

Of those who died, all except one case of eclampsia was in primigravidae, and most were under 25. One was aged 40, and she was the oldest African primigravida ever admitted to Mulago Hospital.

In the whole time only 185 cases of pre-eclamptic toxaemia (including hypertension and chronic nephritis) and 34 cases of eclampsia were admitted—7 cases of eclampsia and 8 of toxaemia died.

Other Causes of Death

There were 53 other causes of death in this series, 49 of which could be classified as only associated with pregnancy:

		Per cent
Cardiac disease	5	9·4
Anaemia	17	34·0
Meningitis	8	13·4
Pneumonia	3	5·6
Cerebral malaria	3	5·6
Peritonitis (non-puerperal)	2	3·8
Urinary disease	2	3·8
Phaeochromocytoma	1	1·9
Unknown	3	5·6
Other (car accidents, etc.)	5	9·4
	49	
Extra-uterine pregnancies over 28 weeks	4	7·5
Total	53	100·0

Cardiac Disease with Pregnancy. This is a very important cause of maternal death in England and Wales, there being 121 cases out of 316 Associated Deaths in 1952–54 (38 per cent). In Mulago there were only 5 out of 49 (10·2 per cent). Only one patient died at full term, the others showing severe failure much earlier. The patients were all admitted in a state of acute failure and were in every case seen, and treatment started, by the physicians.

Anaemia in Pregnancy. There were 17 deaths in this group. The condition is probably confined to certain tropical areas and is of great importance in antenatal care. The patients are usually seen at the clinic complaining of swelling of the feet and ankles and dyspnoea. On admission many are found to have gross oedema of the legs and often of the hands and face. The blood pressure is normal, the urine may or may not contain a little albumin. The haemoglobin is extremely low and in bad cases the gums are so pale that, clinically, it is only just possible to tell where the teeth start—teeth and gums being of the same colour!

Tests show that this is an iron deficient microcytic anaemia and probably due to a multiplicity of causes. The patients have usually had a very poor diet, with practically no meat, eggs or first-class protein. Many suffer from chronic malaria and severe hookworm infection, with much occult blood in the stool. In addition, being pregnant, they have the growing foetus to support. The greatest strain seems to come at about 29–32 weeks, when death usually occurs. Research on this condition is being carried on at the present time in the department and a full report will be published later.

Death Associated with Caesarean Section. Following the lines of the Report on Maternal Deaths in England and Wales, an interesting comparison can be made with deaths following Caesarean section in a community such as this.

It is probably true that many of the patients operated on were in a much worse condition to start with than those in the United Kingdom. In some cases a "quick Caesarean" seemed to give the patient the best chance of living—slender though that chance was. The cases of haemorrhage that died were mostly repeat Caesarean section, perhaps the second, third or fourth operation, and the abdomen was full of gross adhesions, which bled furiously when separated. Sometimes it was not possible to tell if one were in the peritoneal cavity or not—an incision had to be made at the only convenient place, avoiding the bladder and bowel.

There were 775 cases of Caesarean section performed during this time, and 32 died (4·3 per cent). Two deaths were directly attributed to the anaesthetic—there may well have been more. The anaesthetics were practically never given by a qualified doctor; they were administered by a "medical assistant" specially trained to give them. These men are quite adequate in

the routine case, but lack imagination and skill in a really sick or difficult patient. With the shortage of doctors, however, the work could not have been carried on without them. They usually gave a general anaesthetic—gas and oxygen with ether or cyclopropane.

The main reason for performing Caesarean section was disproportion. In nearly every case a trial of labour was given, even for a few hours, to see if normal delivery could take place.

TABLE V

Deaths Associated with Caesarean Section

Total number of Caesarean sections	775
Total number of deaths	32
	No.
Main Cause of Death:	
Sepsis or peritonitis	9
Haemorrhage	8
Shock or collapse	11
Inhalation of vomit	2
Embolus	1
Pulmonary T.B.	1
Total	32
Type of Caesarean section:	
Lower segment	23
Upper segment	9
Total	32
Reason for Caesarean section:	
Disproportion	17
Prolapsed arm or transverse lie	5
Placenta praevia	3
Prolapsed cord	1
Pott's disease	1
Pre-eclamptic toxaemia	2
Large breech	1
Brow	1
Elderly primipara with inertia	1
Total	32
Hours in Labour before Caesarean section:	
Not in labour	6
0–12 hours	6
13–24 hours	9
25–48 hours	5
Over 48 hours	6
Total	32

Owing to the shallow pelvis and late engagement of the head, it is easy to operate prematurely, a mistake often made by newcomers.

The patients who had been in labour for over 24 hours were all admitted from outside. It will be seen that the majority died within 6 hours of delivery—no doubt due to shock with or without haemorrhage.

Pulmonary embolus appears to be a rare cause of death here, and is practically never seen either in the obstetrical, gynaecological or surgical wards among African patients.

CONCLUSIONS

In a review like this, showing such a deplorable waste of life, it is important to keep a sense of balance. Obviously a large number of the deaths were avoidable, due to reluctance on the part of the patient or her relatives to take advice, or to lack of trained doctors and midwives, or to transport difficulties; but slowly with education these are being overcome. Fifteen or twenty years ago, mothers had to be bribed almost to attend antenatal clinics. Last year 41,757 attended the Mulago Clinic alone. There is even greater difficulty in getting suitable girls to train as midwives. The educational standard for girls in East Africa falls sadly below that of boys. The few girls with School Certificate do not want to become nurses, so the standard is generally poor.

The number of maternal deaths is gradually falling and, as more blood becomes available, will drop even more. Comfort must be taken from the fact that 17,279 mothers did not die but went home, for the most part, well and happy.

The greatest single problem that has to be solved here is that of the prevention and treatment of rupture of the uterus. Few places in the world have such a high incidence of spontaneous rupture. Ten years ago the mortality from this condition at Mulago Hospital was 90 per cent. With better facilities this figure has been greatly reduced; whether the number of actual cases has also been reduced is doubtful.

To those of us who work here, there is the constant challenge of difficulties to be overcome, but slowly some headway is being made.

Summary

(1) From January, 1952, to June, 1959, there were 17,519 deliveries at Mulago Hospital, Kampala, Uganda, with 240 maternal deaths—a mortality rate of 13·7 per thousand births.

(2) The commonest cause of death was ruptured uterus—34 per cent, then death from haemorrhage—25 per cent, exhaustion—19 per cent, and sepsis—12 per cent.

(3) Deaths from toxaemia and eclampsia were not so common, being only 8 per cent.

(4) These figures are compared with maternal deaths in England and Wales where toxaemia is commonest, followed by haemorrhage.

(5) The commonest cause of "associated death" in Kampala was anaemia with pregnancy causing death at 28- to 32-weeks gestation.

(6) Seven hundred and seventy-five women were delivered by Caesarean section, with 32 deaths. The main reason was disproportion.

(7) The difficulties that have to be overcome in working in a backward community such as this are discussed.

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THE EFFECT OF INTRAMUSCULAR IRON-DEXTRAN COMPLEX* ADMINISTERED TO WOMEN DURING PREGNANCY ON THEIR HAEMATOLOGICAL VALUES AND ON THE HAEMOGLOBIN LEVELS OF THEIR INFANTS

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INTRODUCTION

THIS paper describes a controlled trial designed mainly to compare the haemoglobin levels of infants born to a random sample of healthy women who received a large dose of intramuscular iron-dextran complex during pregnancy with those who were born to healthy women who had not received any iron medication. The main objective was to see if there was any appreciable increase in haemoglobin value in the infants born to mothers whose iron nutrition had been supplemented. The investigation also provided an opportunity to observe the effects of intramuscular iron on the haematological values in normal pregnancy.

This study was one of a series undertaken during an enquiry into the local prevalence of iron-deficiency anaemia in infancy and childhood (Lanzkowsky and McKenzie, 1959; Lanzkowsky, 1959, 1960, 1961).

There is a voluminous literature, too large for complete review here, on the subject of iron medication in pregnant women. The majority of the reports deal with the effects of the iron administration on the maternal haematological values, and relatively few workers in this field have considered the effects on the infant's haemoglobin level.

A few of the earlier reports consulted on the question of the response to iron treatment in pregnant women are unsatisfactory for various reasons. In several, such as that of Jerlov (1929), there was no control group. In others, for example Davis and Walker (1934), the procedures adopted were unsound or the size of the series inadequate for critical assessment. Other unsatisfactory aspects of the various reports in the literature have been the failure to state the dosage of iron given (Galloway, 1929) or inadequacy of the dosage administered (Davis and Walker, 1934; Richter *et al.*, 1934). A serious pitfall has been failure to take into account the change in haemoglobin level normally occurring in pregnancy as a result of plasma volume changes (Irving, 1935). Since it has often been shown that the haemoglobin level may rise spontaneously during pregnancy, the estimation of this value may not be a reflection of the effectiveness of iron treatment during pregnancy (Elliott, 1940).

Among the acceptable reports is that of Corrigan and Strauss (1936) who, using the Sahli method of haemoglobinometry, observed 200 pregnant women. They treated 100 with 9 gr. ferrous sulphate daily, and the remaining 100 formed a control group receiving no iron medication. The initial haemoglobin levels, determined between the 3rd and 7th month of pregnancy, were 11·2 g. per cent (73 per cent) in the treated group and 11·7 g. per cent (75

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per cent) in the control group. At one week after delivery the mean levels in the two groups were 13·26 g. per cent (85 per cent) and 11·7 g. per cent (75 per cent) respectively. At this stage there were in the untreated group 24 women whose haemoglobin level was below 10·9 g. per cent (70 per cent) whereas in no case in the treated group had the level fallen as low as this. Corrigan and Strauss concluded that adequate iron dosage in pregnancy, especially in the latter months of gestation, may largely prevent hypochromic anaemia in pregnancy.

Many subsequent workers have shown that a rise in haemoglobin level occurs in pregnant women given oral iron, in contrast to the fall often observed in untreated pregnant women (Fullerton, 1936; Toland, 1936; Gottlieb and Strean, 1939; Labate, 1939; Widdowson, 1939). Only occasional workers, such as Adair *et al.* (1936) have failed to demonstrate any difference in mean haemoglobin levels between treated and untreated groups of pregnant women.

More recently, Hamilton and Wright (1942), Benstead and Theobald (1952), Davis and Jennison (1954), Holly (1954), Edgar and Rice (1956), Kerr and Davidson (1958a) and Sturgeon (1959) have all concluded that adequate oral iron medication in pregnancy is followed by a rise in haemoglobin, and the level of haemoglobin usually found in non-pregnant women is maintained throughout pregnancy. The work of these investigators was well controlled, the groups studied were of adequate size, and the procedures adopted were sound.

Fisher and Biggs (1955), studying 138 pregnant women who were treated with 9 gr. ferrous sulphate daily, found that when the initial haemoglobin level was below 90 per cent the administration of oral iron caused it to rise, whilst if the initial reading was over 90 per cent this treatment maintained the high level and prevented the fall that usually occurs in pregnancy. They found that the treatment ensured a high level at term in about 90 per cent of cases. Fisher and Biggs stated that it was their impression that at higher levels of haemoglobin the women were more energetic and tired less easily and were in a better position to withstand haemorrhage and infections.

Oral iron is sometimes poorly tolerated by pregnant women who may have gastric disturbances before therapy is commenced. Scott and Govan (1949) and Benstead and Theobald (1952) have stated that 30 per cent or more of pregnant women suffer from gastro-intestinal upsets during pregnancy and would probably find it difficult or impossible to tolerate ferrous sulphate tablets. This intolerance may be partly psychological (Girdwood, 1952; Kerr and Davidson, 1958a, b). As with any oral medication, it is difficult to ensure that every patient actually takes the prescribed dose. Furthermore, particularly in later stages of pregnancy, urgent correction of anaemia is essential and this cannot be achieved by oral iron.

The introduction of intravenous iron preparations has enabled those patients who cannot tolerate oral iron, or who are still anaemic late in pregnancy, to be treated successfully. Cappell (1930) first showed that iron could be given intravenously as a saccharated iron oxide without the hazards which had often been encountered with parenteral administration of other iron compounds.

This knowledge was not applied clinically until Nissim (1947) reported that he had successfully treated anaemia by the intravenous administration of a stable solution of saccharated iron oxide. Davidson and Girdwood (1948) reported reactions following the use of a solution similar to that used by Nissim but they supported his claim that it could improve the haemoglobin level.

Subsequently Govan and Scott (1949), Kartchner and Holmstrom (1950), Holly (1951), Klopper and Ventura (1951), Scott and Govan (1951) and Briscoe (1952) treated groups of anaemic pregnant women with intravenous iron and all these workers demonstrated very satisfactory increases in haemoglobin level. Govan and Scott (1949), Kartchner and Holmstrom (1950), and Scott and Govan (1951) demonstrated a rise of 1·3 g. per cent, 1·5 g. per cent and 1 g. per cent respectively at one week after the start of treatment. Govan and Scott showed that iron-deficiency anaemia which had proved resistant to iron by mouth improved rapidly with intravenous therapy, but admitted that about 10 to 20 per cent of patients showed a slight general reaction to

intravenous iron and 1 to 2 per cent showed more severe reactions.

Nicholson and Assali (1952), Hagen *et al.* (1954) and Sturgeon (1959) showed a rise in haemoglobin level of 0·7 g. per cent, 1·0 g. per cent and 0·7 g. per cent after the administration of intravenous iron to normal pregnant women. The total dose given by Nicholson and Assali and by Sturgeon was 1,000 mg. of iron intravenously.

The use of intravenous iron therapy has certain drawbacks. It must be administered by a doctor; extravenous leakage is painful; and there may be unpleasant general reactions (Nissim, 1954). For these reasons an iron-dextran complex for intramuscular use has been introduced. This preparation has been most widely used.

Jennison and Ellis (1954) treated 68 anaemic women with 100 mg. of intramuscular iron and demonstrated a mean rise in haemoglobin level of 0·29 g. per cent. Scott and Govan (1954) found a mean rise of 1 g. per cent in 50 anaemic women who were given 500 mg. of intramuscular iron. Both groups of workers concluded that the response to intramuscular iron was comparable to that produced by intravenous iron and that the utilization was of the same order.

There are relatively few reports dealing with the effect on the infant haemoglobin level of the administration of iron to the mother during pregnancy. Gottlieb and Strean (1939) examined the cord blood of 50 infants born to mothers who had not received iron medication in pregnancy and of 50 infants born to mothers treated with iron. At birth the mean haemoglobin level of the infants of the two groups of mothers was 16·80 g. per cent (120 per cent) and 15·44 g. per cent (111 per cent) respectively, and at the end of 32 weeks the values were 7·14 g. per cent (51 per cent) and 11·48 g. per cent (82 per cent) respectively. Gottlieb and Strean postulated that the greater polycythemia present at birth in the infants of untreated mothers was essential for the maintenance of the oxygenation of the foetal tissues, but that the iron storage of the foetus was apparently deficient and the infant could not maintain its normal haemoglobin level during the first year when its growth is most rapid. They omitted certain pertinent and essential information such as the method of haemoglobinometry, birth weight, information on feeding and whether or not prophylactic iron was administered to the infants. For these reasons, despite the fact that the numbers were adequate and the investigation well controlled, this work can be criticized. It does, however, confirm on a large scale the work done by Strauss (1933) who also showed that infants born to anaemic mothers, although normal at birth, developed anaemia during the first year of life. Smallwood (1936), quoting the unpublished results of Gittins, arrived at the same conclusion. Henderson (1942) stated that there was no reason for believing that iron administration to the mother would have any effect in preventing the development of anaemia in her offspring.

Recently Sturgeon (1959) has done extensive work on this subject. In a well-controlled experiment he showed that there was no indication of augmented iron storage in infants born to mothers whose iron nutrition had been supplemented to the extent of achieving abundant reserves. This work is convincing and sound.

Present Investigation

A group of pregnant women were treated with intramuscular iron in dosage calculated to provide an optimal or even superior state of iron nutrition. If this were achieved, observations on a group of infants born to these women should permit valid conclusions to be reached relative to the influence of superior maternal iron nutrition on the offspring. This was the main object of the investigation. It also provided an opportunity to observe the effects of intramuscular iron supplements on the haemoglobin values in normal pregnancy.

Material

A total of 100 Cape Coloured* pregnant women were examined during the sixth and

* The Cape Coloured people are of mixed ethnic origin and descended from various indigenous and imported groups: Slaves, Hottentots, Bushmen, Bantu and Europeans. Ethnically they are "non-White" and their social conditions are similar to those of technically less-advanced communities.

seventh months of pregnancy. They were a random selection of Cape Coloured women attending an antenatal clinic at the Peninsula Maternity Home, which is an institution attached to the University of Cape Town. All these women were given a routine general medical examination at their first attendance and were found to be healthy. Serological tests for syphilis were negative in all. After determination of haemoglobin levels and packed cell volume values, and after the mean corpuscular haemoglobin concentration value was calculated, a quantity of intramuscular iron-dextran complex was prescribed. The dosage was calculated according to the initial haemoglobin level and the body weight.* It was given in bi-weekly injections of 8 ml. (4 ml. into each buttock). Most injections were given personally by the author and no patients complained of excessive pain or discomfort with the large volume of injection material. No undesirable reactions were observed. Intramuscular iron-dextran complex was used since with parenteral therapy the actual amount of iron administered to each patient is accurately known and is not uncertain as it may be with self-administered oral iron treatment.

Only those women who had full-term normal pregnancies, normal labours and who delivered without incident were included. Any women who had haemorrhagic episodes before, during or after delivery were excluded, as were cases of mid-forceps, rotation and breech deliveries or any deliveries requiring anaesthetics.

Of the 100 women initially investigated only 45 received their prescribed iron medication and had normal deliveries of full-term singleton babies in the institution. Of the remainder the majority were defaulters who did not attend for injections despite every effort made to maintain the group as large as possible. The remnant had obstetrical complications, or went into labour prematurely, or were delivered in their homes and for administrative reasons could not be followed. The mean dose of intramuscular iron administered was 20·08 ml. (range 8–32 ml.). This is equivalent to a mean dose of 1,000 mg. of iron.

At term (during the first stage of labour) mean haemoglobin and packed cell volume estimations were determined and mean corpuscular haemoglobin concentration values calculated in the 45 parturient women who had received the total prescribed dose of intramuscular iron. Haemoglobin levels were ascertained in these women between 72 and 96 hours post-partum. The results of the haematological values determined on a random selection of 77 healthy Cape Coloured women at term and after delivery, who had not received any prophylactic iron, were used as control values. Haemoglobin levels in the infants were determined in the first 24 hours of life and at 72 to 96 hours of age. All mothers and infants were followed for 3 months post-partum and at the end of this period the haemoglobin levels in mothers and infants were again investigated. No mother or infant had in the interim received any iron medication. Any infant who had any illness during this period was excluded.

Methods

Blood investigations were done on venous blood in mothers and on capillary blood in infants. The haemoglobin estimations were done by the oxyhaemoglobin method using a Klett-Summerson colorimeter previously calibrated for the purpose against standard haemin and cyanmethaemoglobin solutions. Packed cell volume estimations were made by the standard Wintrobe procedure (Wintrobe, 1929).

Results

The results are shown in summary form in Tables I and II.

It will be noted from Table I that in the treated pregnant women the mean haemoglobin and packed cell volume values were higher at term than at 6 to 7 months' gestation, and higher than the values at term in the control group of untreated women. Both these differences are statistically significant. The rise in haemoglobin value which was observed in the treated group

* The formula used was

$$9W + \frac{W}{6}(100 - \text{Hb. per cent}) = \text{mg. of iron}$$

where W = weight of patient in pounds.
Hb. per cent = observed haemoglobin percentage.
(As recommended by the manufacturers of iron-dextran complex.)

TABLE I

Comparison of Mean Haematological Values in Treated and Control Groups of Pregnant Women

Stage of Pregnancy	Hb. g. %		P.C.V. %		M.C.H.C. %	
	Treated	Control	Treated	Control	Treated	Control
6–7 months (before treatment)	10·68	—	36·10	—	29·81	—
At term	12·08	11·00	41·10	38·87	29·43	28·71

TABLE II

Comparison of Mean Haemoglobin Levels in Treated Cape Coloured Women and Their Infants with Control Groups

Maternal Hb. g. %		Stage	Babies' Hb. g. %	
Treated Mothers	Control Mothers		Of Treated Mothers	Of Control Mothers
10·68	— ..	6–7 months gestation ..	—	—
12·08	11·00 ..	At term: Birth to 12 hours ..	19·23	19·81
—	— ..	13–14 hours post-partum ..	19·20	18·67
10·69	10·18 ..	72–96 hours post-partum ..	18·17	18·34
12·18	11·25 ..	3 months post-partum ..	10·10	10·38

between 6 to 7 months and term is in contrast to the usual finding of a fall in haemoglobin level in the later stages of pregnancy in the absence of iron medication.

For some reason which is not apparent, in the treated women the average mean corpuscular haemoglobin concentration was lower at term than it was before commencement of iron medication. This difference, however, was not statistically significant. The value in the treated group at term was higher than that found in the control group of mothers at term.

Table II shows that at 72 to 96 hours post-partum the difference in mean haemoglobin levels between the treated and untreated groups of women was small. This difference is not statistically significant. At 3 months post-partum the mean haemoglobin level in the treated group was significantly higher than that in the control group, perhaps indicating that the iron treatment had produced a better store of iron for the treated mothers than was available to the untreated ones.

The details of the findings in this investigation are shown in Tables III, IV and V.

Table V shows that the mean haemoglobin level between birth and 12 hours in the infants born to treated mothers was 19·23 g. per cent compared with 19·81 g. per cent in the infants born to the control group of mothers.

The differences between the infants born to the two groups of mothers in respect of their mean haemoglobin levels between birth and 12 hours, 13 and 24 hours, 72 and 96 hours, and at 3 months of age are not significant statistically.

The mean birth weight and weight at 3 months of age in the infants of treated mothers was 6·72 and 11·13 pounds respectively and the corresponding weights of the infants in the control group were 6·94 and 10·84 pounds. The differences in weights in the two groups are not significant statistically.

The umbilical cords of all infants in both groups were clamped at the same interval after birth. The feeding of the two groups was similar, 47·5 per cent of the treated mothers' babies and 45·31 per cent of the untreated group's babies being breast-fed. The average birth weights and weights at 3 months of age, as stated above, were almost identical. In all these

TABLE III

Comparison of Mean Haematological Values at Term and After Delivery in Treated and Control Groups of Women

TABLE III

Comparison of Mean Haematological Values at Term and After Delivery in Treated and Control Groups of Women

	At Term									72–96 Hours Post-partum			3 Months Post-partum		
	Haemoglobin g. %			P.C.V. %			M.C.H.C. %			Haemoglobin g. %			Haemoglobin g. %		
	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.
Treated Group	45	12·08	1·15	39	41·10	4·32	39	29·43	1·62	40	10·69	1·50	38	12·18	0·70
Control Group	77	11·00	1·58	70	38·87	4·59	70	28·71	2·46	66	10·18	1·63	63	11·25	2·43
Significance t:	$p<0·001$			$p<0·02$			$p>0·10$ (N.S.)			$p>0·10$ (N.S.)			$p<0·001$		
F:	$p<0·025$			$p>0·05$ (N.S.)			$p<0·01$			$p>0·05$ (N.S.)			$p<0·001$		

N.S. = Not significant

TABLE IV

Mean Haematological Values at 6 to 7 Months Gestation and at Term in Treated Group of Pregnant Women

	Haemoglobin g. %			P.C.V. %			M.C.H.C. %		
	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.
6–7 months gestation (before treatment) ..	45	10·68	1·14	45	36·10	3·58	45	29·81	1·53
At term	45	12·08	1·15	39	41·10	4·32	39	29·43	1·62
Significance t:	$p<0·001$			$p<0·001$			$p>0·25$ (N.S.)		

N.S. = Not significant

TABLE V

Comparison of Mean Haemoglobin Levels and Mean Weights in Cape Coloured Infants of Mothers Treated with Intramuscular Iron-Dextran Complex and a Control Group of Infants of Mothers Untreated with Iron

	Haemoglobin Level g. %												Weight in Pounds						Feeding		
	Birth–12 Hours			13–24 Hours			72–96 Hours			3 Months			Birth			At 3 Months			Breast-fed %	Artificially-fed %	Complementary-fed %
	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.	No. of Cases	Mean	S.D.			
Treated Group ..	16	19·23	2·09	22	19·20	2·33	40	18·17	1·82	39	10·10	1·05	45	6·72	1·37	39	11·13	1·53	47·50	30·00	22·50
Control Group ..	27	19·81	0·63	50	18·67	0·59	67	18·34	0·59	64	10·38	1·11	74	6·94	0·67	64	10·84	1·79	45·31	32·81	21·87
Significance t: ..	$p>0·25$ (N.S.)			$p>0·25$ (N.S.)			$p>0·25$ (N.S.)			$p>0·10$ (N.S.)			$p>0·10$ (N.S.)			$p>0·25$ (N.S.)					
F: ..	$p<0·001$			$p<0·001$			$p<0·001$			$p>0·05$ (N.S.)			$p<0·001$			$p>0·05$ (N.S.)					

N.S. = Not significant

respects the two groups of infants were strictly comparable.

The conclusion from this investigation is that there is no direct evidence that infants up to 3 months of age benefit by antenatal administration of iron to the mothers if the maternal haemoglobin levels are within the range dealt with in this series.

Discussion

The majority of observers have considered that the anaemia and associated alterations in iron metabolism which occur during pregnancy are manifestations of iron deficiency (Heilmeyer *et al.*, 1941; Young *et al.*, 1946; Cartwright and Wintrobe, 1949; Effkemann and Röttger, 1950; Lundström, 1950; Ventura and Klopper, 1951; Holly, 1953; Sturgeon, 1959).

In normal pregnant women who received no iron supplement the findings of Ventura and Klopper closely paralleled those reported by Sturgeon. They found at term a distinct decrease in haemoglobin concentration as compared with the first trimester. Both studies reported finding associated biochemical changes consisting of a marked increase in serum copper, an increase in free erythrocyte protoporphyrin, a decrease in serum iron concentration and a marked increase in iron-binding capacity. Ventura and Klopper and Sturgeon concluded that these changes represented a shift of values to the brink of iron deficiency in normal pregnancy. Holly (1953) reported similar changes during normal pregnancy. He stated that these changes were more likely to be the result of iron deficiency than of increase in blood volume. Comparable results have been recorded by Laurell (1947), Fay *et al.* (1949), Rath *et al.* (1950) and Holmes (1953). It is evident that during the last trimester of normal pregnancy there are biochemical changes indicative of iron depletion. These changes are comparable to those encountered in iron-deficiency anaemia and in late infancy at which time iron deficiency is prevalent (Sturgeon, 1954, 1956).

Several reports on the effect of oral iron supplements in normal pregnancy were quoted in the introductory part of this paper. The more recent investigators have shown that iron nutrition at term, as judged by haemoglobin concentration, is improved by oral administration of 0·5 to 1·0 g. of ferrous sulphate daily. Similarly it has been shown that parenteral iron administered to pregnant women can maintain the haemoglobin at normal levels and prevent the alteration in erythrocyte morphology and iron metabolism which is so common during normal pregnancy.

Although he made no measurements of total circulating haemoglobin mass, Sturgeon (1959) stated that one could assume from the available evidence that there was an increase in total haemoglobin following the antenatal administration of iron. Lund (1951) observed an average increase in haemoglobin mass of 152 g. in 7 normal women given iron supplements during pregnancy. In 13 controls who did not receive iron supplements an average increase of only 69 g. was found. Mollison (1956) has demonstrated in otherwise normal adults with anaemia that as the venous haematocrit (or venous haemoglobin concentration) increases, there is an associated increase in total red-cell mass (or total haemoglobin mass). In normal pregnancy, when iron supplements are not administered, the increase in blood volume in excess of the increase in haemoglobin mass results in a nett decrease in haemoglobin concentration. According to Sturgeon (1959) it is reasonable to infer from the data which he presented in his study that the increased haemoglobin concentration associated with administration of iron supplements really does reflect an absolute increase in haemoglobin mass.

The question arises whether or not the increase in haemoglobin with therapeutic doses of iron proves that the person was in need of iron. The studies of Vahlquist (1950) indicate that normal non-pregnant women given comparable doses of iron do not achieve any change in haemoglobin or serum-iron concentration. Compared with non-pregnant normal women, therefore, the increases following iron supplements in pregnancy suggest at least a relative deficiency.

It may be logically inferred that increased haemoglobin concentration and the improvement or correction of associated biochemical signs of iron deficiency (Sturgeon, 1959) should be of distinct advantage, although there are no statistically conclusive investigations to prove

this. Many investigators believe that the improved state of iron nutrition is valuable (Davis and Jennison, 1954; Holly, 1954; Fisher and Biggs, 1955; Edgar and Rice, 1956; Gatenby, 1956; Underwood, 1956). Others take the contrary view (Rath *et al.*, 1950; Hytten and Duncan, 1956) and some are undecided (Widdowson, 1939; Magee and Milligan, 1951).

The normal adult male is haematologically stable. In an iron deficiency state injected iron will be quantitatively utilized. The expected rise in haemoglobin can be predicted with reasonable accuracy (Goetsch *et al.*, 1946). In the pregnant woman this does not apply. The demands of the foetus for iron, and the hydraemia of pregnancy, introduce two new variables which make accurate forecasting of haemoglobin levels impossible. In the present investigation the total amount of iron administered equalled approximately 3 to 4 times that required by the average foetus (Widdowson and Spray, 1951) and was a substantial excess over 650 mg., the average maternal requirement during pregnancy (Hytten and Duncan, 1956; Underwood, 1956). In view of this it was thought that this series of pregnant women received an adequate amount of iron and would have an optimal, and possibly in some cases an overloaded, state of iron nutrition.

The fact that the maternal haemoglobin levels and mean corpuscular haemoglobin concentration values in the treated women in the present investigation were only slightly higher than the control group may indicate that the 1,000 mg. of intramuscular iron-dextran complex, which was thought to be an adequate dose to cover any possible maternal and foetal requirements, was actually insufficient and perhaps could have been increased with advantage to the mothers. Nevertheless, a dose of 1,000 mg. of intramuscular iron-dextran complex, which is a considerable addition to the maternal iron, should have been adequate to affect the haemoglobin level of the infant. In the infants of this series of mothers there was no notable rise in haemoglobin level.

Summary

(1) The literature is reviewed as to the effect of the administration of iron during pregnancy on the haemoglobin levels of pregnant women and their infants.

(2) In 45 healthy Cape Coloured women the pre-treatment mean haemoglobin, packed cell volume, and mean corpuscular haemoglobin concentration values at 6 to 7 months of pregnancy were 10·68 g. per cent, 36·10 per cent and 29·81 per cent respectively compared with values of 12·08 g. per cent, 41·10 per cent and 29·43 per cent respectively at term after they had received a mean dose of 1,000 mg. of iron-dextran complex.

Mean haemoglobin and packed cell volume values in the treated women at term were statistically significantly higher than in a control group. The average mean corpuscular haemoglobin concentration value was also higher than the control group but the difference was not statistically significant.

At 3 months post-partum the mean haemoglobin level in the treated women was 12·18 g. per cent compared with 11·25 g. per cent in the control group. This difference is statistically significant.

(3) In the infants born to the treated mothers the mean haemoglobin levels from birth to 12 hours, 13 to 24 hours and 72 to 96 hours of age were 19·23 g. per cent, 19·20 g. per cent and 18·17 g. per cent respectively compared with 19·81 g. per cent, 18·67 g. per cent and 18·34 g. per cent respectively in the infants born to the control group of mothers. None of these differences is statistically significant.

At 3 months of age the mean haemoglobin level in the infants born to the treated mothers was 10·10 g. per cent compared with 10·38 g. per cent in the infants born to the control group of mothers. This difference is not statistically significant.

(4) The conclusion from this investigation is that although iron medication during pregnancy results in a rise in maternal haematological values at term, the mean haemoglobin levels in the infants born to these treated mothers were not significantly higher either at birth, or at 3 months of age, than the mean haemoglobin levels of infants born to mothers untreated with iron.

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THE INFLUENCE OF OESTROGEN AND PROGESTERONE ON THE ELECTROLYTES OF THE HUMAN UTERUS

BY

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AND

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THE present report concerns the effects of oestrogen and of progesterone on the electrolytes of human myometrium. We have used the same methods as in previous studies (Hawkins and Nixon, 1958; Hawkins, Nixon and Whyley, 1958) to estimate extracellular and intracellular levels, employing chloride to measure the extracellular space. The assumptions involved and possible sources of error in this approach have been discussed in the previous reports.

In the previous studies we investigated the changes in electrolyte composition which the myometrium of the human uterus undergoes in pregnancy. In particular, it was found that the myometrial cells become progressively more hydrated as pregnancy proceeds and that the sodium content of the cells increases. In early pregnancy there is also an increase in extracellular water but by the end of pregnancy the myometrial composition alters in such a way that the normal proportion of extracellular water is restored. We also found that, when pregnancy is complicated by pre-eclampsia, a pathological increase of extracellular water and electrolytes occurs in late pregnancy, and myometrial intracellular sodium levels are increased.

In order to deduce the mechanism of the changes in myometrial electrolytes occurring in pregnancy and the possible causation of pathological modifications of electrolyte composition, it is necessary to know what are the effects of oestrogen and progesterone on uterine electrolytes. Such data as are available (Talbot, Lowry and Astwood, 1940; Horvath, 1954; Daniel and Daniel, 1957; Bitman *et al.*, 1959) have been obtained with rats, rabbits and cats, and are partly contradictory. In order to interpret the changes in the electrolyte content of the human myometrium during pregnancy, it is essential to obtain information, using the same methods, on the effects of oestrogen and progesterone on the human uterus. Electrolyte analyses of small biopsies of myometrium from non-pregnant and pregnant patients undergoing various operative procedures after treatment with oestrogen or progesterone have therefore been undertaken.

The doses of hormones which we have employed may well be small in relation to the endogenous production during pregnancy. Although only limited numbers of suitable cooperating patients were available, the results of this work gave information on the action of oestrogen and progesterone on myometrial electrolytes which is of assistance in the interpretation of the changes occurring in pregnancy.

METHODS

Biopsies of the myometrium were taken during laparotomies performed under general anaesthesia at a time when no oxytocic drugs had been given. At the same time specimens of heparinized blood were obtained by venepuncture. The subsequent treatment of the specimens, the analytical methods, and the computations of intracellular electrolytes were

the same as those in a previous study (Hawkins and Nixon, 1958). The results of the electrolyte analyses were expressed per 100 g. dry tissue and averaged for each group of patients studied. The standard deviations quoted in the tables represent chiefly variation between patients, the variation in the estimates of the electrolyte content of different samples of myometrium from the same site being relatively small.

In order to assess the effect of oestrogen or progesterone on the electrolyte composition of the myometrium, the results from the various groups of hormone-treated patients in the present study were compared with control values obtained previously from comparable groups of untreated patients (Hawkins and Nixon, 1958). For the comparisons "t" tests were employed. In general changes demonstrable at the $P=0{\cdot}05$ level were considered significant.

Sites of Biopsy

In patients having the operation of hysterectomy the whole uterus was available for study. The material used was classified in the following way: (*a*) specimens from the *corpus uteri*; that is, that part of the uterus lying above the level of the internal os; (*b*) specimens taken at the level of the internal os; (*c*) specimens from the cervix.

With two patients who were undergoing sterilization by the abdominal route small biopsies were taken from the *corpus*. In patients having a plastic repair of a malformed uterus the resected tissue was available. In the case of patients having hysterotomy for termination of pregnancy or Caesarean section, small biopsies were taken from the edge of the incision.

Cases Studied

(1) *Non-pregnant*. Three patients were given progesterone, 75 mg./day intramuscularly in divided doses for 48 hours before operation. Two patients had hysterectomy with salpingo-oöphorectomy, one for recurrent carcinoma of the breast, the other for a small left tubal recurrence of a previously extirpated carcinoma of the right ovary. The third had a plastic repair of a bicornuate uterus and incompetent internal os. The uterus was histologically normal in these cases. The operations were carried out on the 19th, 7th and 27th days of the cycle respectively.

Five patients were treated with oestrogen before operation. The operations performed and the doses of oestrogen given were as follows: (*a*) Hysterectomy for chronic pelvic pain, endometriosis left broad ligament, cystic ovaries, two seedling fibromyomata. Oestradiol benzoate 10 mg. daily intramuscularly for 48 hours. (*b*) Sterilization 6 days after therapeutic abortion for pulmonary tuberculosis. Oestradiol benzoate 10 mg. daily intramuscularly for 4 days. (*c*) Plastic repair of incompetent internal os. Oestradiol benzoate 15 mg. daily intramuscularly in divided doses for 48 hours. (*d*) Vaginal hysterectomy for post-menopausal procidentia. Oestradiol benzoate 5 mg. daily intramuscularly for 48 hours; stilboestrol pessaries. (*e*) Sterilization (for psychosis) 4 days post-partum. Stilboestrol 5 mg. twice daily orally for 3 days. Case (*a*) was operated upon on the 11th day, Case (*c*) on the 18th day of the cycle.

(2) *Early pregnancy*. Three patients having abdominal hysterotomy for termination of pregnancy were treated pre-operatively with progesterone. The durations of the pregnancies were 10, 11 and 16 weeks, and the indications for termination were psychosis, pulmonary tuberculosis and leprosy respectively. Each of these patients was given 50 mg. progesterone 6-hourly intramuscularly for 48 hours pre-operatively.

Three other patients were given oestrogen before their pregnancies were terminated at 11, 20 and 26 weeks for psychoneurosis with suicidal tendency, schizophrenia and leprosy respectively. Each was given oestradiol benzoate 50 mg. 12-hourly intramuscularly for 48 hours pre-operatively.

(3) *Pregnant, at term*. Three patients having elective Caesarean section at 39 to 40 weeks of pregnancy were given progesterone. The indications for section were contracted pelvis with two previous abdominal deliveries, bad obstetric history with three previous abdominal deliveries, and myomectomy during the current pregnancy, respectively. Each of these three patients was given progesterone, 50 mg. 6-hourly intramuscularly for 48 hours before operation.

Four patients having elective Caesarean section at term for transverse lie, previous

prolapse repair, and cephalopelvic disproportion with previous Caesarean section (2 cases), respectively, were pre-treated with oestrogen. Each was given oestradiol benzoate 50 mg. 12-hourly intramuscularly for 48 hours pre-operatively.

None of the patients from whom biopsies were taken had pre-eclampsia; none had gone into labour before operation. In no case pre-treated with hormones was the patient's clinical course detectably altered by this pre-treatment. All had uneventful post-operative courses.

Results

Non-pregnant

The number of patients available for study was too small to make allowance for the phase of the menstrual cycle at which the operation took place. The days on which the operations were conducted were randomly distributed throughout the cycle. This was also the case with the group of untreated patients with which the present groups were compared.

The principal changes in electrolyte composition of the myometrium in response to hormone administration observed in the present study occurred in the group of non-pregnant patients treated with oestrogen. They consisted of an increase in the water content of the myometrium, and an increase of calculated intracellular sodium. The data for the myometrium of the *corpus* are shown in Table I. It will be seen that the increase in water content produced by oestrogen was confined to the intracellular space and resulted in an increase in intracellular water concentration from 490 to 641 g./kg. intracellular phase. The calculated intracellular sodium rose from 1·2 to 9·5 m.eq./100 g. dry tissue. These changes are of the same order as those occurring in pregnancy (Hawkins and Nixon, 1958). On the other hand, we previously observed that, in early pregnancy, extracellular space and extracellular water were increased, though normal again at term. Short-term administration of oestrogen did not reproduce this change.

The effect of oestrogen in increasing total water, intracellular water and intracellular sodium was confirmed ($P<0·05$, $<0·1$, and $<0·1$ respectively) when the results from these cases were compared with those from progesterone-treated cases. In a few specimens from the level of the internal os, a similar comparison showed a higher total water content with oestrogen, the values being 382 (oestrogen) and 302 g./100 g. dry tissue (progesterone) respectively. In a single specimen of cervix from a patient given oestrogen, the calculated extra-

Table I

	Controls	Oestrogen	Progesterone
Total water (g./kg. wet tissue)	795 ± 9 (5)	816 ± 6 (4)	794 ±12 (3)
Total water (g./100 g. dry solids)	389 ±23 (5)	444 ±18 (4)	386 ±29 (3)
Extracellular water (g./100 g. dry)	293 ±22 (5)	274 ±26 (3)	261 ±18 (3)
Intracellular water (g./100 g. dry)	96 ±27 (5)	173 ± 7 (3)	125 ±31 (3)
Intracellular water concentration (g./kg. I–C phase)	490 ±67 (5)	641 ± 8 (3)	555 ±58 (3)
Extracellular phase (g./100 g. dry) (=chloride space)	295 ±22 (5)	277 ±26 (3)	264 ±18 (3)
Total chloride (m.-eq./100 g. dry)	35·0± 3·3 (5)	34·7± 3·4 (4)	32·1± 2·6 (3)
Total sodium (m.-eq./100 g. dry)	42·5± 2·4 (5)	51·2± 8·1 (4)	40·1± 3·4 (3)
Total potassium (m.-eq./100 g. dry)	29·6± 3·5 (5)	31·5± 6·5 (4)	30·8± 5·6 (3)
Total calcium (m.-eq./100 g. dry)	6·1± 3·3 (4)	8·6± 5·7 (3)	4·1± 1·5 (3)
Total magnesium (m.-eq./100 g. dry)	4·7± 3·1 (4)	5·8± 1·3 (3)	4·5± 1·1 (3)
Intracellular sodium (m.-eq./100 g. dry)	1·2± 2·6 (5)	9·5± 5·4 (4)	2·2± 2·1 (3)
Intracellular potassium (m.-eq./100 g. dry)	28·4± 3·6 (5)	30·3± 6·6 (4)	29·6± 5·6 (3)
Intracellular calcium (m.-eq./100 g. dry)	5·4± 3·2 (4)	7·9± 5·7 (3)	3·7± 1·5 (3)
Intracellular magnesium (m.-eq./100 g. dry)	4·4± 2·9 (4)	5·4± 1·3 (3)	4·2± 1·2 (3)

Note.—All specimens of myometrium from the *corpus* of non-pregnant uterus. Mean values, standard deviations and numbers of cases are indicated.

cellular (chloride) space was 353 g./100 g. dry tissue compared with values of 274 and 276 respectively in two cases pre-treated with progesterone. We are reluctant to interpret these values for chloride space as truly representing extracellular space in a tissue such as cervix, which contains so much fibrous tissue.

Progesterone administration produced no major changes in electrolyte composition of myometrium from non-pregnant patients (see Table I). It was clear that the rise in extracellular space which occurs in early pregnancy (Hawkins and Nixon, 1958), could not be accounted for by the sole influence of progesterone in the amounts given in the present work. The values for extracellular space and extracellular water were in fact lower ($P<0{\cdot}1$) in the progesterone-treated cases than in the controls.

Early Pregnancy

The only consistent change in electrolyte composition in this group of cases was in biopsies from the *corpus uteri* of patients pretreated with progesterone. It consisted of a reduction in the intracellular sodium level. The mean value obtained in the control groups was 5·3 m.-eq./100 g. dry tissue, while that in progesterone-treated groups did not differ significantly from zero. As has been pointed out in a previous publication (Hawkins and Nixon, 1958) the reason these values are so low is probably due to a slight systematic overestimation of extracellular space volume as measured by the uncorrected chloride space. The two values for intracellular sodium quoted are, however, comparable and it is likely that progesterone administration causes a true fall in intracellular sodium during early pregnancy.

Pregnant, at Term

No significant changes in myometrial water, sodium or potassium levels were detected in the cases studied. Administration of either oestrogen or progesterone appeared to cause some reduction in total and intracellular calcium and magnesium levels, in specimens from lower segment of the uterus. The few upper segment specimens available showed similar changes. These results are shown in Table II.

Discussion

We have shown that administration of oestrogen to non-pregnant women causes an increase in total water in the myometrium. This change appears to be confined to the intracellular compartment and is accompanied by an increase in the sodium content of the myometrial cells. The fact that in the pregnant state where myometrial intracellular water and sodium are already increased (Hawkins and Nixon, 1958) we were unable to demonstrate any further increase merely suggests that the doses of oestrogen used were small in comparison with the enhanced endogenous production of pregnancy.

Table II

	Controls	Oestrogen	Progesterone
Lower Segment:			
Total calcium (m.-eq./100 g. dry)	8·5± 4·3 (10)	5·8±2·3 (4)	3·6±1·1 (3)
Intracellular calcium (m.-eq./100 g. dry) ..	7·7± 4·3 (10)	5·0±2·3 (4)	2·9±1·0 (3)
Total magnesium (m.-eq./100 g. dry)	5·9± 2·0 (10)	3·6±1·4 (4)	4·2±1·2 (3)
Intracellular magnesium (m.-eq./100 g. dry) ..	5·5± 1·9 (10)	3·4±1·4 (4)	3·9±1·2 (3)
Upper Segment:			
Total calcium (m.-eq./100 g. dry)	13·2±10·5 (2)	9·9±6·5 (2)	2·9 (1)
Intracellular calcium (m.-eq./100 g. dry) ..	12·5±10·5 (2)	8·7±5·7 (2)	2·2 (1)
Total magnesium (m.-eq./100 g. dry)	10·3± 8·2 (2)	3·3±3·5 (2)	5·1 (1)
Intracellular magnesium (m.-eq./100 g. dry) ..	9·9± 8·0 (2)	3·2±3·5 (2)	4·8 (1)

Note.—All cases pregnant, at term. Mean values, standard deviations and numbers of cases are given.

Progesterone, 75 mg./day, did not appear to influence the myometrial electrolytes of non-pregnant women. Of course, with such a small number of patients minor responses are easily overlooked, but the results do suggest that no major change in myometrial electrolytes occurred consistently. Progesterone did appear to reduce intracellular sodium in early pregnancy —it may be that the effect is only seen when the amounts of this ion have been increased in consequence of pregnancy. It is almost certainly true that the doses of progesterone we gave, though large by customary standards, were small compared with the enhanced endogenous production in pregnancy. Hayden (1958) found that administration of 1,000 mg. of progesterone per day was sufficient to produce a material increase in the pregnanediol output of pregnant women.

A few results from animal experiments are available for comparison with the present findings. Talbot *et al.* (1940) investigated the effect of oestrogen on the uterus in immature rats. Their results are compatible with ours. Rises in total and intracellular water were observed, and it may be computed that a rise in intracellular sodium content occurred. Daniel and Daniel (1957) deduced that the increase in uterine water caused by oestrogen was associated with expansion of the intracellular compartment relative to the extracellular space in both rabbits and cats. Talbot *et al.* and Daniel and Daniel used samples of whole uterus for their determinations and the results are open to the criticism that changes in the myometrium and the endometrium are not necessarily parallel. In fact, both Horvath (1954) and Bitman *et al.* (1959) found that electrolytes in the two tissues responded in different ways to hormone administration. Both these authors used ovariectomized rabbits as controls and found that in these circumstances oestrogen causes increases in extracellular water and cellular potassium, changes we did not observe in human myometrium. In other respects the results of Horvath differ from those of Bitman *et al.*, probably due to differences in method. The latter authors were unable to detect any significant changes in intracellular water or intracellular sodium in the myometrium of rabbits treated with oestrogen or progesterone. Walaas (1950) has shown that in castrate rats oestrogen administration causes some increase in content of calcium and magnesium. It will be noted from Table I that our mean values for these two ions in the oestrogen-treated non-pregnant uterus are higher than those in controls. In our cases the changes were not statistically significant.

The discrepancies between the animal experiments and our own are probably due to both species difference and differences in method. In mentioning species difference we do not necessarily imply that there is any fundamental difference between the myometrial cell of the rat or rabbit and that of the human. A difference in the cellular composition of the muscular layer of the uterine wall such as different proportions of connective tissue cells and stroma would be quite sufficient to account for variation in electrolyte content and its changes in response to hormones. In particular, the significance of the chloride and residual spaces is altered by the presence of different amounts of connective tissue (see Manery, 1954) and consequently values for "intracellular" electrolytes deduced from them are not comparable from species to species. Among the details of method which may be involved is the possible influence of endogenous hormonal status at the time of the experiment—the castrate animal may differ in its electrolyte responses from the animal with normal ovarian activity. Differences in analytical procedures, methods used to estimate extracellular space, and computation of intracellular levels, may all play a part.

It is for these reasons that the effects we have demonstrated are strictly valid only for the interpretation of changes in the electrolyte composition, determined by the same methods, of human myometrium from comparable patients. It was for this purpose that the experiments were designed.

Changes in Human Myometrial Composition in Pregnancy

It will be seen that the increases in myometrial intracellular water and sodium levels which occur in pregnancy (Hawkins and Nixon, 1958) can be accounted for by increased endogenous oestrogen production. Administration of oestro-

gen to non-pregnant women causes similar changes. With the data from the present study we are unable to account for the increase in myometrial extracellular fluid which occurs in early pregnancy.

It is of interest to note that in the groups of cases studied in early pregnancy progesterone administration caused some reduction in calculated intracellular sodium. This finding is compatible with the view that the raised myometrial intracellular sodium of pre-eclampsia (Hawkins *et al.*, 1958) is related to a relative deficiency of progesterone production in this condition.

Summary

(1) Analyses for water and electrolytes were conducted on biopsy specimens of human myometrium taken at operation. Intracellular levels of water and of the cations were calculated using "chloride space" to estimate the extracellular phase.

(2) In non-pregnant patients, administration of oestrogen caused an increase in myometrial water content, which appeared to be confined to the intracellular phase, and an elevation of the calculated intracellular sodium level.

(3) In early pregnancy administration of progesterone caused a fall in the calculated intracellular sodium level of the myometrium.

(4) In late pregnancy myometrial calcium and magnesium were lower in cases treated with oestrogen or progesterone than in untreated controls.

(5) It is considered that the increases in myometrial intracellular water and sodium levels which occur in pregnancy (Hawkins and Nixon, 1958) can be attributed to the effects of increased endogenous oestrogen.

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A TRIAL OF TWO ORAL DIURETICS AND BED REST ON URINARY ELECTROLYTE EXCRETION IN OEDEMA OF PREGNANCY

BY

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DIETARY restriction of salt intake has been widely used as an adjuvant to the treatment of mild pre-eclampsia, especially among patients admitted to hospital. It is also advised for out-patients with obvious oedema but no other signs warranting admission. If there is any logic in the treatment of pre-eclampsia and oedema by salt restriction, the same logic should apply to increasing salt elimination by saluretic agents, provided it is as efficacious and there are no dangerous side-effects.

Chlorothiazide is a potent diuretic now widely used in general medicine for oedema of all varieties, including that of renal origin. Its primary action is to increase excretion of chloride (Slater and Nabarro, 1958). There is initially an approximately equimolecular excretion of sodium and chloride, and the diuretic effect appears to be secondary to the electrolyte excretion. Its main disadvantage is that it often causes hypokalaemia (Slater and Nabarro, 1958; Bayliss *et al.*, 1958). Other side-effects are dizziness and nausea (Barfield *et al.*, 1958), and thrombocytopenia (Nordqvist *et al.*, 1959). One case of agranulocytosis (Zuckerman and Chazan, 1958) has been reported.

By causing a slight reduction in blood volume, chlorothiazide will potentiate many hypotensive agents, an action shared by other diuretics. When given by mouth, there is only slight carbonic anhydrase inhibition (Assali *et al.*, 1958). Chlorothiazide, therefore, does not have the same tendency to cause harmful acidosis as does Acetazolamide, a powerful inhibitor of carbonic anhydrase, which has been used for oedema of pregnancy.

Hypokalaemia can be produced by most diuretics, even Mersalyl, when given intensively, particularly in the presence of a restricted salt intake. It has been related to carbonic anhydrase inhibition and aldosterone secretion.

Chlorothiazide has been used in the treatment of oedema of pregnancy and pre-eclampsia (Donald, 1959; Tennent and Leslie, 1960). Finnerty *et al.* (1958) have compared its effect with that of acetazolamide. They concluded that chlorothiazide was more effective, but that a combination of the two produced the greatest result. They claim definite improvement in hypertension and albuminuria even in quite severe cases. This has not been confirmed by other workers (Assali *et al.*, 1958). These workers and others (Barfield *et al.*, 1958) do find a significant improvement in oedema of pregnancy.

Hydrochlorothiazide is an hydrogenated derivative of chlorothiazide, which differs only in the presence of two extra hydrogen atoms in the thiadiazine ring of the molecule (de Stevens *et al.*, 1958). It is weight for weight approximately ten times more potent than chlorothiazide (Havard and Fenton, 1959), and has also been used in the treatment of pre-eclampsia (Sears, 1960).

Hydrochlorothiazide is reported (de Stevens *et al.*, 1958) to have *in vitro* even less carbonic anhydrase inhibitory effect than chlorothiazide and, hence, less tendency to cause excretion of bicarbonate (Fleming *et al.*, 1959; Platts, 1959).

This means that there is even less likelihood of harmful acidosis occurring during treatment.

It was hoped likewise that hydrochlorothiazide might not have the same tendency to produce a potassium deficiency. Animal studies (de Stevens *et al.*, 1958) suggested that this might be the case and such was indeed the first clinical impression (Richterich, 1959). However, Fleming *et al.* (1959), Kerr *et al.* (1959) and Platts (1959) all report a potassium excretion equivalent to that of chlorothiazide. Havard and Fenton (1959) add that in acute oedema the potassium loss is not nearly as significant as that occurring in chronic oedema of long standing, particularly in patients on a restricted salt intake.

The Trial

A trial has been conducted to compare the effects of hydrochlorothiazide, chlorothiazide and bed rest in 10 patients with oedema of pregnancy, some of whom also had other signs of pre-eclampsia. The patients were all admitted to hospital before the 38th week of gestation. This limit was chosen as many of the patients would have been induced at term, if not before, and the trial took fourteen days to complete.

No patients with albuminuria at the onset were included as the chances were that they would not complete the course before delivery. The patients were divided alternately, in order of admission, into two groups. The first group, after an initial period of bed rest, were given chlorothiazide first and hydrochlorothiazide second. The second group, after a similar preliminary period, were given the hydrochlorothiazide before the chlorothiazide.

It is well known that if two diuretics are administered consecutively, the second diuretic is at a disadvantage in that its measurable effect is less. If, therefore, two drugs which have a disproportionate action are tested and the more powerful is used first, any difference will be magnified. Similarly, if the weaker is used first, any difference will be diminished. A comparison of the results of alternation should therefore reveal any significant difference.

Two other patients were withdrawn from the trial. In both cases this withdrawal occurred before the exhibition of the drugs and so alternate administration was not interrupted. The first patient spontaneously ruptured her membranes and shortly went into labour at 36 weeks. The second was admitted at 36 weeks with pre-eclampsia and within 24 hours developed signs of imminent eclampsia and required urgent Caesarean section.

Method

It was decided to conduct the trial under the normal conditions for treatment of pre-eclampsia, as far as possible. Urine collection started at 8.0 a.m. on the day following admission, and was continued for 12 days. In accordance with the current practice, a normal hospital diet was allowed, except that added salt was forbidden. Also the bed rest was not absolute, except for patients with albuminuria or hypertension sufficient to cause concern.

Normal drug treatment was not interfered with. This only amounted to sedation with barbiturates in all cases except one of essential hypertension with superimposed pre-eclampsia, who was treated with reserpine by injection.

Investigations

The patients were weighed daily, at the same time each day, in the same garment and an effort was made to see that their bowels had moved beforehand.

Blood pressure was recorded daily in the routine way, but as the investigation was not primarily concerned with this no special arrangements were made.

The 24-hour urinary output was collected in special containers each day for 12 consecutive days. From each 24-hour collection an aliquot was removed and the concentrations of sodium and potassium were estimated by flame photometry and hence the total daily output of these elements was calculated and expressed in mille-equivalents per 24 hours.

Similarly the chloride concentration was estimated by titration by the method of Van Slyke and Hiller (1947).

All patients were rested in bed for four days without treatment as a control period and to establish a steady state. The first diuretic was

then administered at 10.0 a.m. and 2.0 p.m. for three days. Following this, there was a recovery period of two days and then the second diuretic was administered at the same time for the next three days.

The doses used were chlorothiazide 500 mg. b.d. and hydrochlorothiazide 50 mg. b.d.

The Patients

There were 3 multigravidae and 7 primigravidae. Of the latter one had twins, and one suffered from essential hypertension which was treated by reserpine. Six patients, at the time of the trial, had signs of pre-eclampsia other than oedema. In 8 cases labour was artificially induced.

One patient (E) was investigated at 30 weeks with oedema alone. She was re-admitted at 36 weeks with mild hypertension and recurrence of oedema. Although the results on this second occasion were not included in the series, she was given the diuretics in the reverse order after a similar period of bed rest. Her blood pressure did not exceed 140/90 after the second day but there was a trace of albumin in the urine on the 3rd, 5th and 10th days. She was discharged on a maintenance dose of hydrochlorothiazide. At 39 weeks foetal movements ceased, and eventually she was delivered of a stillborn breech weighing over 8 pounds. A glucose tolerance test showed a pre-diabetic type of curve. The hypertension and albuminuria had not recurred.

In one other patient (H) it was possible to observe that albuminuria developing during the trial became progressively more severe.

Results

For the purposes of the trial, the excretion values on the 4th day of the rest period have been corrected to an arbitrary zero, from which other readings have been expressed as variants. Two patients showed a considerable excretion on the first day of rest. The output rapidly tailed off, which is why, for averaging purposes, the 4th day value has been taken as steady.

Figure 1 shows a comparison of the average chloride excretion of the two series of patients superimposed on each other.

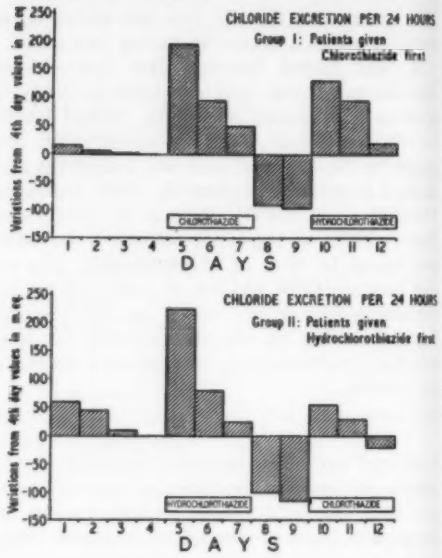

Fig. 1

Average chloride excretion expressed as a variation from fourth day resting values.

Figure 2 shows the average sodium excretion expressed in the same way.

The total change produced by treatment is perhaps best assessed by considering the weight changes.

Table of Weight Changes

(1) Average weight change during the initial period of rest =gain of 0·7 pounds.

(2) Average change during 3 days of first diuretic treatment:

(*a*) Chlorothiazide =loss of 3·4 pounds.

(*b*) Hydrochlorothiazide =loss of 4·0 pounds.

(3) Average change during recovery period of 2 days =gain of 2·2 pounds.

(4) Average change during 3 days of second diuretic treatment:

(*a*) Chlorothiazide =loss of 1·6 pounds.

(*b*) Hydrochlorothiazide =loss of 2·2 pounds.

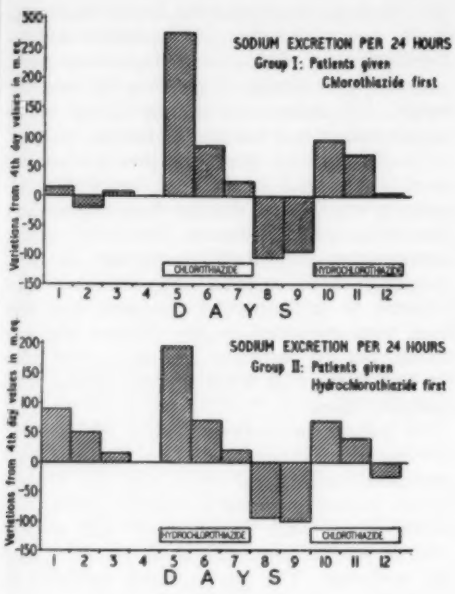

FIG. 2

Average sodium excretion expressed as a variation from fourth day resting values.

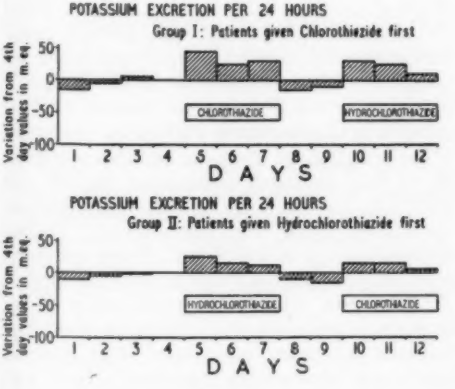

FIG. 3

Average potassium excretion expressed as a variation from fourth day resting values.

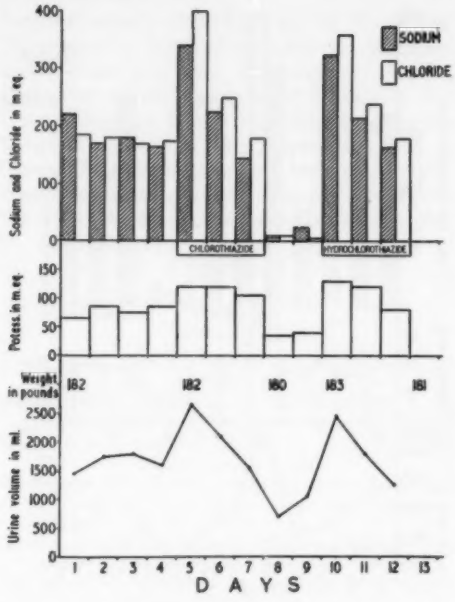

FIG. 4

Patient E. Admitted at thirty weeks.

Chart showing weight changes, urinary volume and electrolyte excretion.

Figure 3 shows a comparison of the average potassium excretion in the 2 groups as before.

Figure 4 shows the individual results for patient E admitted at 30 weeks.

Figure 5 shows the results for the same patient treated in the reverse order at 36 weeks.

CONCLUSION

Bearing in mind the fact that alternation of the order of exhibition of the drugs should accentuate any difference between them, the results show that, at the dosage used, a virtually identical response in terms of electrolyte excretion occurs. There is a marked increase in electrolyte excretion over the resting value. In the recovery period, after withdrawing the drugs, sodium and chloride very nearly disappear from the urine. During this period all patients, except

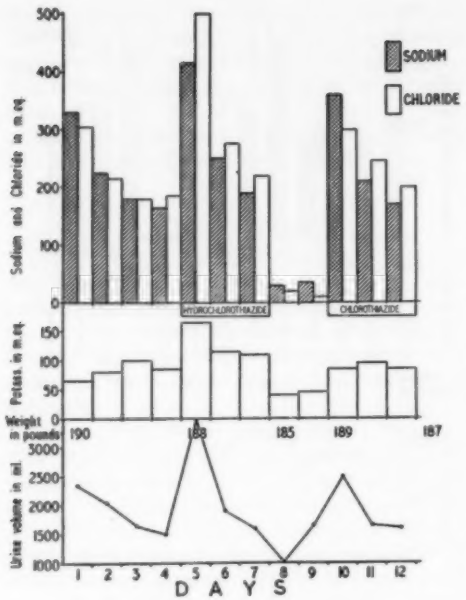

FIG. 5

Patient E. Admitted at thirty-six weeks.

Chart showing weight changes, urinary volume and electrolyte excretion.

one, gained weight rapidly, sometimes regaining all the weight lost during the first diuretic period.

The weight changes show a slight bias in favour of hydrochlorothiazide but the difference is not statistically significant for the small number of patients involved. This is not to say that it may not be real, but it would require a larger trial to demonstrate a small difference of this order.

The second diuretic did not cause such a marked weight loss as the first, often not reducing completely the gain in the recovery period. It should be remembered, however, that even in the absence of pre-eclampsia and oedema, pregnant patients gain weight throughout, due largely to the increase in size of the uterus and to its contents. It was noticed that in nearly all cases clinical oedema demonstrably improved during the initial period of bed rest. Nevertheless it seems that this improvement was chiefly due to the change in position and redistribution of fluid from dependent parts, because the majority of patients did not lose weight, and, indeed, the average change was a weight gain of 0·7 pounds for the four days.

Finally, although the blood pressure was not specially recorded for the purposes of the trial, ordinary ward testing did not show any obvious correlation with treatment. The only serious hypertension was that of patient G, who seemingly had essential hypertension. The response to intramuscular reserpine may well have been enhanced by the diuretic she was taking, but no particular rise was noted after the end of the trial when she was treated with reserpine alone.

No patient deteriorated rapidly while taking the diuretics. Patient J developed more acute pre-eclampsia after the end of the trial. Patient H was treated on a unit in which a more conservative approach is practised and it was obvious that the albuminuria progressed during the treatment. The one stillbirth occurred in patient E, who was treated twice and also given out-patient diuretic therapy. It is not possible to state whether the stillbirth was related to the use of diuretics, but this accident has been described in patients treated with these drugs (Watt and Phillip, 1960).

Retention of fluid and electrolytes is a feature of pre-eclampsia, and evidence has been offered (Dieckmann, 1950) that, in certain cases, intravenous injection of 2·5 per cent saline has caused a marked deterioration in the disease. It is logical to use dietary restriction or artificial increase in elimination as part of the treatment. What is clear from this case, and that of patient H, is that increased elimination of salt and fluid did not obviate the basic pathology of the disease. Such treatment, although causing an amelioration of symptoms, should not therefore interfere with the traditional treatment of pre-eclampsia, namely the termination of the pregnancy whenever the hazards of birth and neonatal life seem no greater than those of continued intra-uterine existence. There is a danger that a false sense of security may be engendered.

The excretion of potassium does not parallel

the excretion of the other electrolytes. No difference between the two drugs was noticed. There was not an increase in the second period. No symptoms of hypokalaemia were produced in this trial. This does not preclude the possibility of hypokalaemia in prolonged therapy particularly in the presence of a salt-restricted diet. If interrupted treatment is given to counter this possibility, the figures suggest that a latent period of not more than one day should be used, otherwise there will be an almost complete restoration of lost weight between diuretic episodes.

Summary

Ten patients with oedema of pregnancy or pre-eclampsia with oedema were treated with bed rest and then two oral diuretics. A definite increase in the excretion of sodium and chloride over the resting values was noted. There were concomitant weight changes.

Any difference between the two diuretics, used in the dosage specified, was not statistically significant.

There was one stillbirth and one patient in whom the pre-eclampsia obviously progressed.

It may be concluded that both these diuretics produce a similar and significant effect on oedema of pregnancy, as compared with bed rest. With regard to pre-eclampsia, there was some evidence that the disease could progress during their use and it would require a larger trial of different type to determine whether they can influence the foetal salvage. No side-effects were encountered in this trial.

Acknowledgments

I thank Dr. M. Sandler for help and encouragement and for allowing me the freedom of the Biochemical Department of the Bernhard Baron Memorial Research Laboratories, where all the estimations were carried out; Dr. R. G. Spector for help and advice on the many technical aspects of the trial; Mr. M. P. Curwen, Department of Medical Statistics, St. Bartholomew's Hospital, and Professor J. H. M. Pinkerton of the Institute of Obstetrics and Gynaecology at Queen Charlotte's Maternity Hospital, for advice; the Consultant Staff of Queen Charlotte's Maternity Hospital for permission to investigate their patients; Mr. N. K. Harrison, Department of Medical Photography, St. Bartholomew's Hospital, for assistance in the preparation of the figures.

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METABOLIC CHANGES IN ACID-BASE BALANCE OF THE BLOOD DURING PREGNANCY, AT DELIVERY AND POST-PARTUM

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THE occurrence of compensated changes in acid-base balance of the blood during normal pregnancy is generally agreed upon. As early as 1928, Oard and Peters (1929) found in the course of an electrolyte and alkaline reserve study on the blood of pregnant women, the appearance of a concomitant and equal reduction in anions and total base. The primary driving force, responsible for these compensated changes, is assumed by some authors to be the change in respiration occurring in pregnant women and described as physiological hyperventilation (Myers *et al.*, 1932; Goodland *et al.*, 1954; Boutourline-Young *et al.*, 1956). The relevant available data suggest that variations in the respiratory rate are not due to an increase in CO_2 as a result of a rise in metabolic rate, but to the continuous effect of nervous stimuli brought about through pregnancy. The ensuing, prolonged fall of alveolar CO_2 tension causes a decrease in plasma bicarbonate. Thus, the primary respiratory disturbance in acid-base balance is followed by metabolic changes which are secondary (Gaebler and Rosene, 1928; Dieckmann and Wegner, 1934; Nice *et al.*, 1936; Plass and Oberst, 1938).

This opinion, though prevalent, is opposed by another group of investigators who claim that accumulation of abnormal acids in the blood occurs during pregnancy and labour (Siedentopf, 1931). The subsequent changes in respiration which cause a "wash off" of CO_2 are compensatory by resulting in a relative increase in buffer base.

It was thought that an investigation of the metabolic changes in acid-base balance in the course of pregnancy and at delivery, could provide information as to the body's compensatory ability and its deterioration in an unsteady state. Therefore, the object of the present study was twofold:

(1) To examine the metabolic changes in acid-base balance of the blood in the same subject throughout the course of pregnancy.
(2) To observe in how far the muscular activity at labour affects the steady state as compared with the post-partum period.

METHODS

The investigation was carried out on 20 healthy pregnant women divided into two

groups. The first group included 8 pregnant women who volunteered for a monthly venous blood sampling, as from the 5th month of pregnancy. The last blood sample in this group was obtained at the end of the first stage of delivery.

Twelve additional pregnant women volunteered only after admission to hospital for delivery. Three blood samples were obtained from every woman in this group. The first was taken at the beginning of labour, as determined by the opening of the uterus cervix to 1–2 cm. and the occurrence of birth contractions. The second sample was obtained at the end of the second stage of labour, while the last was taken 24–30 hours after labour.

The blood samples were withdrawn from a vein into siliconized 30 ml. sterile syringes containing a drop of heparin solution of 5,000 U/c.cm. to which a solution of 10 per cent sodium fluoride in a final concentration of 0·1 per cent was added. Samples for haematocrit determinations were taken before introducing the fluoride solution.

Acid-base balance in the blood was estimated according to Brewin *et al.* (1955). Five ml. portions of each blood sample were equilibrated in 230 ml. tonometers with pCO_2 ranging from 20 to 80 mm. Hg in air, during 15 minutes in a water bath at 37° C. The blood was then withdrawn in an air-free syringe and its CO_2 content was determined using the manometric Van Slyke apparatus. The pH of the blood was measured by a Cambridge pH meter with a Stadie electrode system at 37° C. and buffer at pH 7·37. The pCO_2 of the gas phase in the tonometer was determined by the Haldane gas analysis apparatus. With the results obtained, log pCO_2 was plotted against log vol. per cent CO_2 and log pCO_2 against pH.

Concomitant shifts in both plots indicated metabolic changes in acid-base balance. Figure 1 gives a graphic interpretation of the results.

Oxygen capacity was determined in the portion of blood equilibrated at approximately 40 mm. Hg pCO_2 in air.

In the group examined only during delivery, estimation of lactic acid was made by the application of the *enzymatic method* of Wieland (1958).

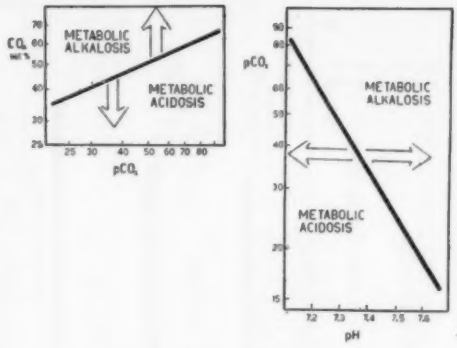

FIG. 1

Graphic interpretation of shifts indicating metabolic changes in acid-base balance.

Control determinations were carried out on 5 healthy non-pregnant women in the basal state.

RESULTS

Subjects from the first group, examined in the course of pregnancy and at delivery, showed individual differences in each of the two states. No definite trend deviating from the normal was observed in the CO_2 absorption or in the pH/log pCO_2 curves, during the course of pregnancy. In the last sample obtained at the end of the first stage of delivery, changes in both curves indicated the development of metabolic acidosis. In this sample the fall in CO_2 content at pCO_2 40 mm. Hg was found to be in the range of 41·0 to 45·8 vol. per cent, while the pH at pCO_2 40 mm. Hg ranged from 7·225 to 7·355. Changes in CO_2 content at pCO_2 40 mm. Hg are demonstrated in Figure 2.

In the second group of experiments, carried out on subjects admitted to hospital for delivery, the following results were obtained. The first blood sample taken at the beginning of the first stage showed a CO_2 combining power, at pCO_2 40 mm. Hg, in the range of 41·5 to 47 vol. per cent; the range of pH at the same

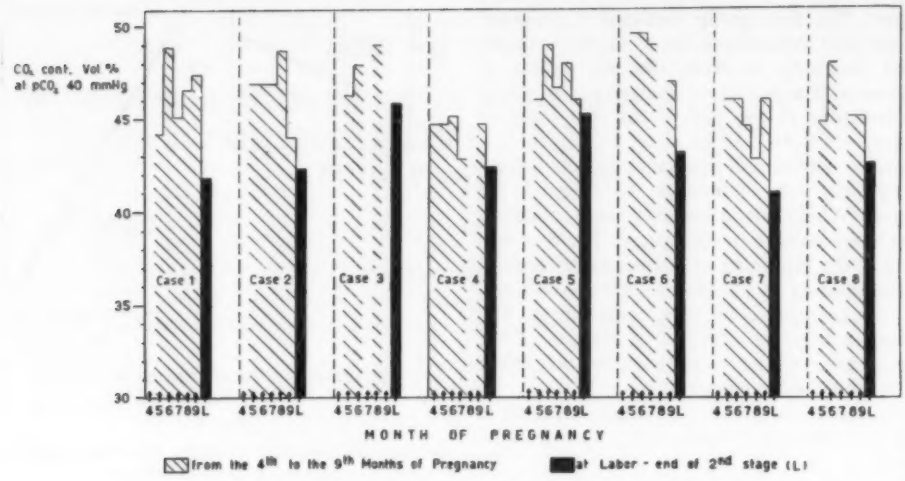

FIG. 2

CO_2 content in equilibrated blood at pCO_2 40 mm. Hg. Samples obtained from subjects examined throughout the course of pregnancy.

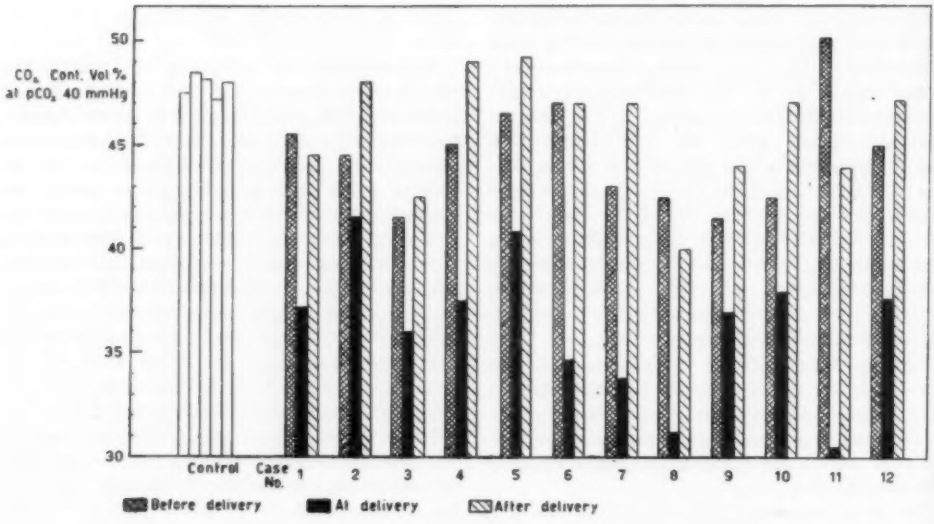

FIG. 3

CO_2 content in equilibrated blood at pCO_2 40 mm. Hg. Samples obtained from subjects admitted to hospital for delivery.

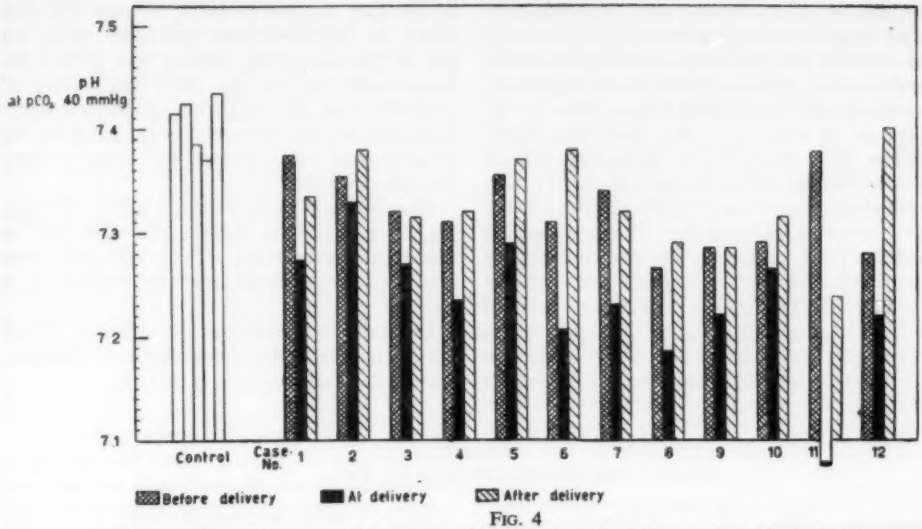

FIG. 4

pH of equilibrated blood at pCO_2 40 mm. Hg. Samples obtained from subjects admitted to hospital for delivery.

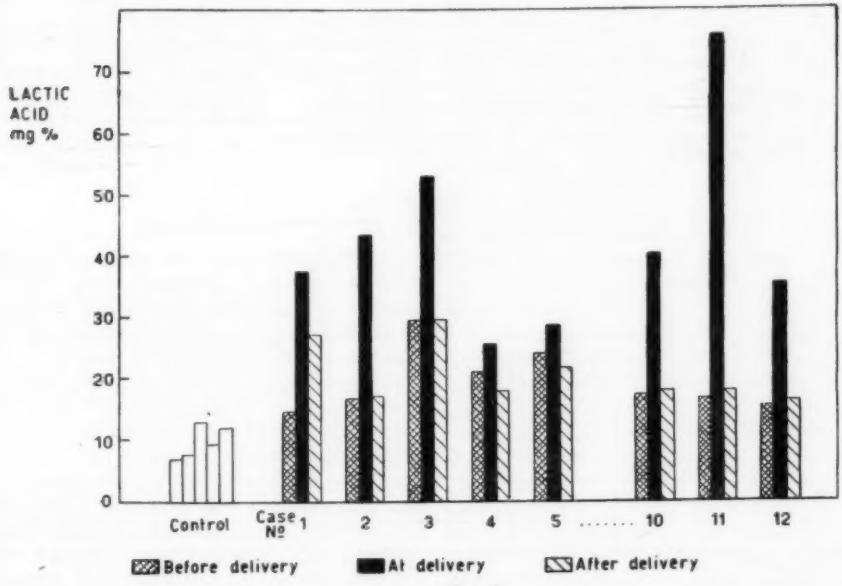

FIG. 5

Blood lactic acid mg. per cent. Samples obtained from subjects admitted to hospital for delivery.

CO_2 tension being 7·265–7·375. The difference in the range of findings at this stage of delivery, as compared with the range in the findings from the first group, taken at a later stage of delivery, is noteworthy. Lactic acid values were in the range of 14·6 to 29·5 mg. per cent. Blood samples taken at the end of the second stage of delivery showed a significant fall in the CO_2 combining power and a shift of the pH/log. pCO_2 curve to the acid side. The range of the results at pCO_2 of 40 mm. Hg was CO_2 content between 31·2 and 41·5 vol. per cent, and pH 7·073–7·330. Lactic acid rose to a range of 25·5–53 mg. per cent. Blood samples taken 24–36 hours after delivery showed a considerable recovery towards the previous values. The range of the CO_2 content at pCO_2 40 mm. Hg was found to be 40–49 vol. per cent, while the pH at the same CO_2 tension was 7·20–7·38. Lactic acid fell to the pre-delivery level of 16·3–29·7 mg. per cent. During labour haemoconcentration was observed as indicated by the simultaneous increase in O_2 capacity and haematocrit value.

Changes in CO_2 content at pCO_2 40 mm. Hg, in pH and in content of lactic acid in blood, as against the values obtained from controls, are demonstrated in Figures 3, 4 and 5.

Clinical data concerning the subjects, as well as the results of all determinations obtained, are tabulated in Tables I, II and III.

TABLE I

Blood Examination Throughout Pregnancy

Subject	Age	Pregnancy No.	O_2 Capacity Volume % at Month of Pregnancy						End 2nd Stage Labour	CO_2 Content Volume % at pCO_2 40 mm. Hg at Month of Pregnancy						End 2nd Stage Labour
			4th	5th	6th	7th	8th	9th		4th	5th	6th	7th	8th	9th	
S.D.	23	First	—	16	15·8	15·7	—	17·6	17·2	—	44·2	48·9	45·1	46·6	47·4	41·8
S.G.	28	Third	—	17·6	17·6	—	—	20	18·2	—	46·9	46·9	46·9	48·7	44	42·3
Z.M.	19	First	—	15·6	14·7	—	12·9	—	16·8	—	46·3	47·9	—	49	—	45·8
A.M.	34	Third	16·5	—	13	15·5	—	18·2	16·6	44·7	44·7	45·1	42·8	—	44·7	42·5
J.Z.	26	Second	—	15·2	12·9	13·9	15·5	17·1	17	—	46	49	46·7	48	46	45·2
C.R.	23	First	—	15·1	14·7	16·9	—	15·3	18·4	—	49·6	49·6	49	—	47	43·2
C.M.	28	Second	—	17·5	—	17·8	17·1	16·1	16·7	—	46	46	44·6	42·8	46	41·0
Z.R.	19	First	—	17·9	15·6	—	15·4	15·4	16·5	—	44·8	48	—	45·1	45·1	42·6

In all cases—head presentation.

TABLE II

Blood Examination from Onset of Labour Through Post-partum Period

Subject	Age	Pregnancy No.	Labour Hours	Haematocrit			O_2 Capacity Volume %			CO_2 Content Volume %			pH†			Blood Lactic Acid mg.		
				1*	2*	3*	1*	2*	3*	1*	2*	3*	1*	2*	3*	1*	2*	3*
N.S.	20	First	23	32·8	37·4	31·3	17·9	18·9	16·6	45·5	37·2	44·5	7·375	7·275	7·335	14·6	37·6	27·2
M.A.	18	First	24	27·8	35·5	34·5	17·7	18·7	17·8	44·5	41·5	48	7·355	7·330	7·380	16·7	43·5	17
H.P.	24	First	10	35·3	38·5	39	18·4	20·7	19·4	41·5	36	42·8	7·320	7·270	7·315	29·5	53	29·7
A.J.	22	First	16	35·5	39·3	29·6	17·9	18·7	13·6	45	37·5	49	7·310	7·235	7·320	21	25·5	18
S.J.	19	First	14	25·5	30	21·8	17·7	18·1	15·1	46·5	40·8	49·2	7·355	7·290	7·370	24	28·6	21·8
A.L.	20	First	14	29·3	26·5	30·7	18·5	18·8	15·7	47	34·7	47	7·310	7·205	7·380			
S.C.	19	First	11	26·2	33·3	25·5	13·9	16·1	12·4	43	33·8	47	7·340	7·230	7·320			
A.E.	22	First	24	29·5	31·5	27	16·9	17·2	15·9	42·5	31·2	40	7·265	7·185	7·290			
J.J.	25	First	17	26	30	23	16·1	18·1	15·1	41·5	37	44	7·285	7·220	7·285			
L.M.	20	First	12	37	36·6	36·3	16·1	17·3	16·6	42·5	38	47·1	7·290	7·265	7·315	17·4	40·2	18·1
R.A.	20	First	12	30	42	—	14·5	15·3	14·3	50·2	30·5	44	7·380	7·085	7·240	16·5	76	18
H.B.	22	Second	6	31·2	41·7	36·5	16·6	19·8	18·8	45	37·7	47·2	7·280	7·225	7·400	14·7	35·4	16·3

In all cases—head presentation.

1*, 2*, 3*=blood samples.

1*—at first stage of labour.

2*—at delivery.

3*—24–36 hours after delivery.

† CO_2 content and pH values at pCO_2 40 mm. Hg.

TABLE III

Control Examination of Blood

Subject	CO_2 Content Volume % at pCO_2 40 mm. Hg	pH at pCO_2 40 mm. Hg	Blood Lactic Acid mg. %
T.S. ..	47·5	7·415	7·0
H.R. ..	48·5	7·425	7·8
T.Z. ..	48·1	7·385	13
S.A. ..	47·2	7·370	9·4
S.M. ..	48	7·435	12

In the control group the range of CO_2 content of equilibrated blood at pCO_2 40 mm. Hg was found to be 47·7–48·5. It should be recalled that equilibration was carried out at normal body temperature, 37° C., which explains the difference between these values and the normal alkaline reserve values given in the literature. The range of pH at the same pCO_2 was between 7·37 and 7·435. Control values of lactic acid in blood were in the range of 7–13 mg. per cent. The above results, arrived at by the application of Wieland's enzymatic method, tally with values given by other authors (Long, 1924; Cook and Hurst, 1933).

DISCUSSION

The results of the investigation show that no particular trend deviating from the normal prevails in the changes in acid-base balance of the blood throughout the course of pregnancy. There was a slight irregular shift of the log pCO_2/log CO_2 content and of the pH/log pCO_2 "lines" either to the alkaline or to the acid side, which could be interpreted as normal variations. Considering the acid-base balance of the blood as an expression of the homeostasis of the human body, a lack of any definite deviation in the changes denotes a state of equilibrium in the internal environment of the body in pregnancy. This conclusion is corroborated by the results of other investigators concerning changes in electrolytes and pH of the blood, who consider the simultaneous change in bicarbonate and serum proteins without accumulation of organic acids and variation in H^+ concentration as an expression of a compensatory change occurring during pregnancy (Oard and Peters, 1929; Stander *et al.*, 1929; Kydd, 1931; Muntwyler *et al.*, 1931; Oberst *et al.*, 1940). Keeping in mind the difference in the accuracy of estimation of the various blood components, the right to balance results obtained on anion—and cation—concentrations appears questionable. The method used in this investigation appears to give the final figure in the acid-base equilibrium of the blood. Even more, with experiments carried out at a temperature of 37° C., it prevents misinterpretations likely to arise from physico-chemical alterations in blood components due to differences between body and experimental temperature at the time of determination (Brewin *et al.*, 1955).

In the second group of experiments on subjects admitted to hospital, a definite metabolic acidosis was found at the time of delivery, which was an expression of the unsteady state in the body. This acidosis originated mainly in the accumulation of lactic acid. Moreover, in some of our experiments the observed fall at term in the CO_2 combining power, expressed in meq, corresponded to the simultaneous rise in lactic acid of the blood. The correlation of these two findings could serve as a criterion of proper care of the patient, since it should not be overlooked that delivery can also be accompanied by starvation and water imbalance, which by themselves would induce accumulation of acid anions in the blood, resulting in another aspect of metabolic acidosis.

The accumulation of lactic acid at delivery was already established by Schultze (1926) and Bokelmann (1927), by application of the Clausen method for lactic acid estimation. However, considering the conclusions arrived at by Long (1924) and by Owles (1930), according to which estimation by the Clausen method showed merely one-half to two-thirds of the true lactic acid, Bokelmann's figures would appear lower than, though qualitatively similar to, our own.

As to the source of the lactacidaemia, it is felt that this point requires further discussion.

It is well known that lactic acid derives from carbohydrates or the carbohydrate fraction of protein molecules. It is a normal product of muscular metabolism, oxidized and re-synthesized to glycogen during the recovery phase of muscular contraction. It appears in blood when muscular exercise is performed under limited supply of oxygen to the muscles, which can be a result of either low oxygen tension or a decrease in the total amount of oxygen reaching them. The latter state occurs in vigorous muscular contraction, when shortening of muscular fibres interferes with the regular blood supply.

Delivery is obviously accomplished by vigorous contraction of the skeletal muscles of the abdominal wall and diaphragm, and the simultaneous contractions of the smooth muscles of the uterus. In respect of the skeletal muscles, Barcroft and Swan (1953) have shown that stasis occurs during strong, sustained contraction, thus affecting their normal oxygen supply. Hence the skeletal muscles contracting at delivery would be one source of lactic acid accumulation, while the contracting uterus could be assumed to be another source. Woodbury *et al.* (1938) have measured the pressure variations resulting from uterine contractions under normal conditions, as against those prevailing at the time of delivery. The average maximal tension of the uterine wall was calculated from the figures obtained. In normal conditions, the maximum tension of the uterine wall was found to be 500 g./cm.^{2} of wall area, while at the time of delivery the propulsive force rose to 15 kg./cm.^{2}. As to the uterine blood flow under these conditions, experimental data on sheep and dogs have shown that the contractions of the uterus are accompanied by a significant decrease in blood flow. Moreover, when contractions are of tetanic nature, uterine ischaemia is severe (Assali *et al.*, 1958).

With regard to metabolic changes occurring in the contracting smooth muscle, direct experimental evidence is scarce. In the present investigation a metabolic acidosis was observed right from the first stage of labour, which is characterized by contractions of the uterine musculature solely, whilst the abdominal skeletal muscles are still at rest. It therefore could be assumed that contracting smooth muscles of the uterus produce the rise in lactic acid. Similar findings at this stage of labour have been obtained by Bokelmann (1927) in his study of blood lactic acid levels in pregnancy and labour.

Despite the conclusions drawn from our studies, the controversial findings of Kerridge and Winton (1929) should be recalled. In their experiments on anaesthetized cats and rabbits, experimental production of full contraction of the uterus perfused with pituitary extract caused no change in the pH of the muscle, nor was accumulation of acid observed.

Summary

Metabolic changes in acid-base balance of the blood have been investigated throughout the course of pregnancy, at delivery and post-partum. There was no definite deviation from the normal during pregnancy. A metabolic acidosis due mainly to accumulation of lactic acid was found at the time of delivery. The source of the lactacidaemia is discussed.

Acknowledgments

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KIELLAND'S FORCEPS ROTATION IN THE FIRST STAGE OF LABOUR

BY

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AN occipito-posterior position of the vertex may cause prolonged and painful labour, sometimes ending in a difficult forceps delivery and occasionally Caesarean section, even though the pelvis is adequate for a normal delivery with an occipito-anterior position.

AETIOLOGY

The occiput may be directly posterior, or may lie posteriorly with the sagittal diameter in one or other oblique diameters of the pelvis. According to Whitridge Williams (1930) this was found early in labour in 11·3 per cent of 5,488 cases. The head often engages in the lateral position, but these cases are not under consideration here.

The incidence of an occipito-posterior position is less frequent than would be accounted for by chance, or by the position of the placenta. The foetus has an inherent tendency to assume a flexed attitude and the easier accommodation of the ventral surface of the foetus over the forward convexity of the lumbar spine discourages the posterior position of the foetal back. It is stated that the high head with the occipito-posterior position is due to poor cephalic flexion, which prevents engagement, but it may well be that a high head tends to favour a posterior position. It is difficult to believe that the shape or size of the pelvic brim has much influence on the position of the engaging head although it is more likely that it will engage with the sagittal suture running antero-posteriorly with an anthropoid pelvis. A high angle of inclination of the pelvic brim may delay engagement of the head, and may sometimes be found with an occipito-posterior, but there is no real correlation between any pelvic abnormality and an occipito-posterior position.

THE MYTH OF POOR FLEXION

In all the textbooks the poorly flexed head with an occipito-posterior is held to be the cause not only of a high head before labour, but also of delay in descent, because a larger engaging diameter produces a relative disproportion at all levels of the bony pelvis. Incoordinate uterine action has also been attributed to the poorly flexed head.

Although it is undoubtedly true that the lower cervical spine (C.4.5.6.) is markedly extended with an occipito-posterior before the onset of labour and in early labour the head is nevertheless well flexed if it is considered solely in relation to the pelvis (Fig. 2). Even when there is a long and painful first stage of labour radiograms (Figs. 4, 5 and 6) show that the engaging diameter is usually the suboccipito-bregmatic and that there is less than 10 degrees of extension at the occipito-cervical joint (Fig. 1). Difficulty and delay in the first stage of labour cannot be attributed to non-existent disproportion or to a badly flexed head.

With an occipito-anterior the foetal axis

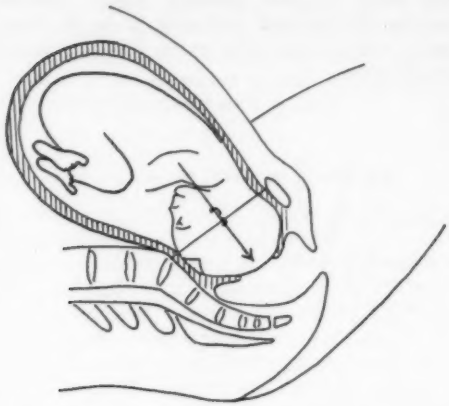

FIG. 1

Occipito-anterior vertex presentation engaged in the pelvic brim. The foetal axis pressure is directed downwards and backwards in line with the axis of the birth canal.

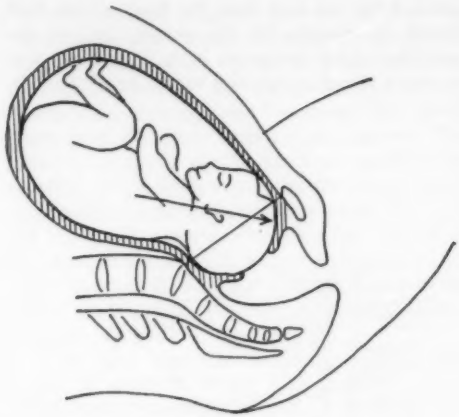

FIG. 2

Occipito-posterior vertex presentation engaged in the pelvic brim. The foetal axis pressure is directed forwards at 45 degrees to the axis of the birth canal on to the anterior wall of lower uterine segment and back of the symphysis pubis.

pressure is directed on to the cervix in the axis of the birth canal (Fig. 1). With an occipito-posterior the foetal axis pressure is directed forwards at about 45 degrees to the axis of the birth canal on to the anterior wall of the lower uterine segment and the back of the symphysis pubis (Fig. 2). This would account for the frequent association between the occipito-posterior position and the posterior unripe cervix. When labour begins much of the expulsive forces are expended against the symphysis pubis and in consequence cervical dilatation is slow. The urethra is compressed and catheterization may prove difficult. The anterior lip of the cervix may become nipped and progressively oedematous in the absence of radiological evidence of disproportion.

At Queen Charlotte's Maternity Hospital in 1956, 1957 and 1958 there were 161 cases of labour lasting more than 48 hours. In 126 (78·3 per cent) the foetal head was occipito-posterior at the onset of labour. In 79 cases the head had failed to rotate to the anterior position at the end of the 2nd stage. Although the posterior position cannot be blamed for all cases of prolonged labour it is nevertheless such a common association that it clearly has a marked effect upon the efficiency of the uterus and is the main cause of so-called incoordinate uterine action. As the head descends on to the

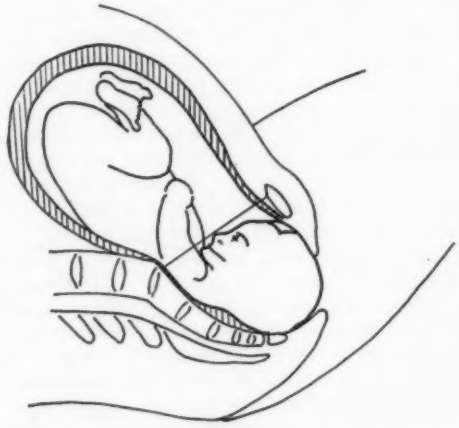

FIG. 3

Occipito-posterior vertex presentation at the outlet of the pelvis. Further flexion of the head on the trunk is taking place.

pelvic floor not only does the head remain well flexed in relation to the pelvis, but as the shoulders enter the pelvic brim the foetal spine becomes flexed in relation to the head (Fig. 3). The myth of poor cephalic flexion persists because the anterior fontanelle is in the fore-pelvis and is thus more easily felt on vaginal examination.

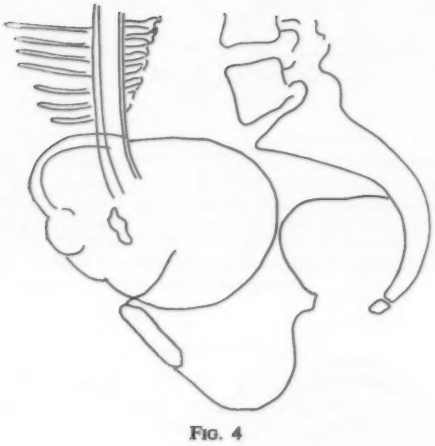

FIG. 4

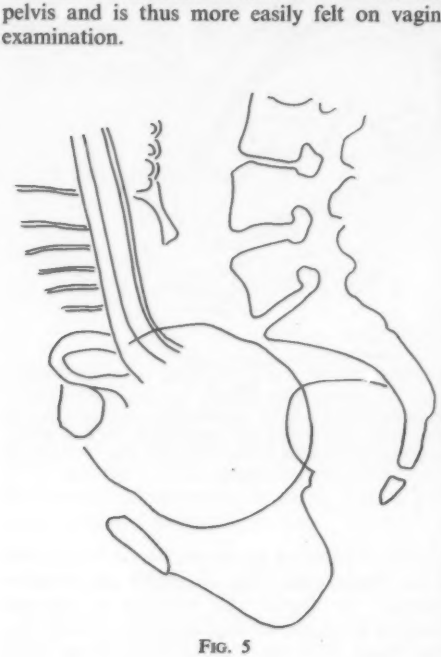

FIG. 5

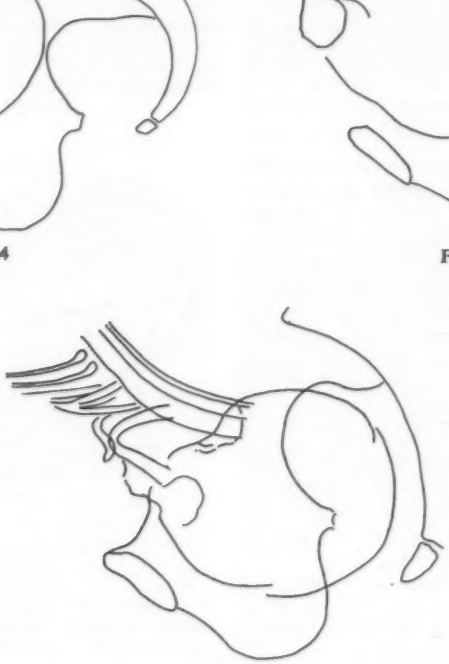

FIG. 6

FIGS. 4, 5 AND 6

Radiogram tracings showing occipito-posterior vertex presentations. Note that the foetal axis pressure is directed forwards against the back of the symphysis pubis.

Poor flexion and even extension of the head to a brow presentation may be found after engagement of the head, but as a rule this only occurs in a capacious pelvis, and it is not necessarily associated with dystocia.

Failure of Internal Rotation

It is well known that internal rotation of an occipito-posterior head often occurs when the head has reached the pelvic floor. The cause of this internal rotation has usually been attributed to the occiput reaching the pelvic floor first, and the erroneous belief in a poorly flexed head fitted well with Berry Hart's gutter-shaped pelvic floor theory to explain why the head sometimes fails to rotate from the direct occipito-posterior position. With a persistent occipito-posterior it is difficult to believe that the sinciput actually leads and is rotated to the front, and it is doubtful if posterior rotation of the occiput often occurs. Chassar Moir (1932) revived Sellheim's (1907) theory of unequal foetal flexibilities to explain forward rotation of the occiput as the head descends through the forward curve of the lower birth canal and this we accept.

Failure of internal rotation may be due to failure of the head to descend as far as the pelvic curve. A narrow transverse diameter of the pelvis may prevent rotation, and the rotation force is weak when the pelvis has only a slight curve. Thus a persistent occipito-posterior is commonly seen with an anthropoid pelvis. The rotation force is weak with a direct occipito-posterior, just as it is with a weight balanced on top of a wheel, because rotation forces are acting equally on each side of the head.

Delivery Face-to-Pubis

With an occipito-anterior the head is delivered by a movement of extension which is easy, whereas with the fully flexed occipito-posterior the head has to be expelled by further flexion, which is difficult, or even impossible once the shoulders have engaged in the pelvic brim (Fig. 5).

Expulsion of the head from the birth canal with the occiput posterior is more difficult than with the occiput anterior because the occipito-frontal diameter of the fully flexed head has to come through the vulva instead of the suboccipito-frontal, and because the wider biparietal diameter emerges posteriorly. This results in arrest of the head or marked distension of the pelvic floor with the risk of severe lacerations extending into the rectum. Rotation of the head, spontaneously or by manual or forceps assistance, will permit extension of the head around the forward concave curve of the lower birth canal. Easy vaginal delivery is then usually achieved.

It is often said that moulding of the foetal head is different when the head has been delivered face-to-pubis instead of with the occiput anterior, but we have found no evidence to support this view.

Management

Attempts to correct an occipito-posterior position during the antenatal period are not recommended but early in labour, before the head has engaged, the back is encouraged to rotate to the front if the patient lies in the Sims' or semi-prone position, on the side opposite to the foetal back, and the patient may experience considerable relief of pain when this position is adopted.

Most obstetricians agree with Chassar Moir (1956) who knows of no evidence to justify early interference, and every opportunity should be given for the cervix to reach full dilatation spontaneously. Hunter (1953), however, advocated manual rotation in prolonged labour before full dilatation of the cervix, but this can only be achieved late in the first stage and it is not possible to draw the head down on to the cervix during the final stages of rotation.

Malmström (1957) has used a vacuum extractor cup. This will pull the head down on to the pelvic floor, but tends to slip on the scalp when rotation is attempted.

In the belief that rotation of the head would accelerate dilatation of the cervix when the first stage is prolonged, one of us (J.M.H.) has practised rotation of the head with Kielland's forceps when the cervix is less than half dilated.

TABLE I

Occipito-posterior Positions Rotated with Kielland's Forceps During the First Stage of Labour

No.	Previous Viable Pregnancies	Duration of Pregnancy	Duration of Labour: Before Kielland Rotation (Hours)	Duration of Labour: Before Kielland Rotation (Minutes)	Duration of Labour: After Kielland Rotation (Hours)	Duration of Labour: After Kielland Rotation (Minutes)	Cervical Dilatation at Time of Rotation	Method of Delivery	Weight: Pounds	Weight: Ounces	Remarks
1 ..	0	41	42	10	3	10	¼	Normal	6	3	
2 ..	0	38	36	20	4	0	3 fingers	Low forceps	7	4	
3 ..	1	43	32	15	1	20	¼	Low forceps for foetal distress.	10	3	
4 ..	1	42	38	40	1	45	3 fingers	Low forceps	9	8	Oxytocin drip
5 ..	0	42	36	0	2	30	3 fingers	Low forceps	7	4	Continuous epidural block
6 ..	0	40	52	0	4	0	3 fingers	Midcavity forceps	7	12	
7 ..	0	41	42	0	–	10	¼	Kielland forceps delivery with anterior lip of cervix	8	2	
8 ..	0	39	56	40	3	40	¼	Midcavity forceps	7	7	
9 ..	0	38	51	0	1	10	¼	Midcavity forceps	8	1	
10 ..	0	37	36	10	4	0	3 fingers	Normal	7	0	
11 ..	0	40	49	30	6	10	3 fingers	Further rotation from ROL and midcavity forceps	6	8	
12 ..	0	40	43	15	3	15	3 fingers	LSCS for P.O.P. and foetal distress with cervix two-thirds dilated	7	3	Continuous epidural block. Contracted funnel pelvis
13 ..	0	41	37	20	3	5	3 fingers	Midcavity forceps	7	1	
14 ..	0	39	46	10	8	5	3 fingers	LSCS for P.O.P. Cervix still 3 fingers dilated	8	15	
15 ..	0	41	54	15	–	10	¼	Kielland forceps delivery for foetal distress	8	2	Small cervical laceration sutured
16 ..	0	36	37	10	4	0	¼	Low forceps	6	4	

KIELLAND ROTATION IN THE FIRST STAGE OF LABOUR

Sixteen cases of prolonged labour, each associated with an occipito-posterior position, were selected because vaginal delivery seemed unlikely and each if left alone would probably have needed a Caesarean section. None had exceeded 4–6 cm. (3 to 4 fingers) of cervical dilatation. Under general anaesthesia Kielland's forceps were carefully applied through the cervix. After obtaining a perfect cephalic application the head was slightly elevated and then slowly rotated between contractions to the occipito-anterior position. The head was then gently pulled down on to the cervix before removing the forceps. The shoulders invariably follow the head (Scott and Gadd, 1957) and over-correction discourages a return to the posterior position. Two cases reverted to a posterior position and were subsequently delivered by Caesarean section. Fourteen cases achieved full dilatation within 4 hours and were delivered *per vaginam*. No babies were lost. The following case history is typical:

Mrs. A.S., aged 18 years, primigravida, was examined when 17 days over term with a view to surgical induction. The cervix was posterior and the cervical canal was so tightly closed that induction was not possible. Labour began spontaneously later the same day. Following 24

hours of strong labour, necessitating the administration of Pethidine 350 mg., chloral hydrate gr. 60, Omnopon gr. ½ and scopolamine gr. 1/150, the cervix was 1 cm. dilated. The membranes had ruptured and the liquor was meconium-stained. A continuous lignocaine epidural block was effectively maintained for 10 hours but then became ineffective. After 36 hours of strong labour the cervix was now 4 cm. dilated. Under general anaesthesia Kielland's forceps were applied through the cervix and the head which was in a direct occipito-posterior position was rotated slowly between uterine contractions through 180° to the direct occipito-anterior position. The forceps were removed and a further intramuscular injection of Pethidine 200 mg. was given to relieve the labour pains. After a further 2½ hours of labour full cervical dilatation was reached and a low forceps delivery was completed. The infant weighing 7 pounds 4 ounces cried at birth.

Kielland's forceps rotation may be attempted in the first stage of labour when there is undue delay, but it is not recommended as a routine method of management of the occipito-posterior position in prolonged labour. Nevertheless, correction of the occipito-posterior position does appear to overcome the so-called incoordinate uterine action and to assist rapid cervical dilatation.

When there is delay in the second stage of labour delivery will always be easier if the occiput is first rotated to the front, whether the head is high in the cavity or on the pelvic floor.

Summary

Difficult labour with an occipito-posterior position is believed to be due to mal-direction of the foetal axis pressure, and not to poor flexion of the head. Rotation to the occipito-anterior position with Kielland's forceps during a prolonged and difficult first stage has overcome the dystocia. Rotation is always advised if there is delay in the second stage of labour.

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A SEQUENTIAL TRIAL OF ANALGESICS IN LABOUR

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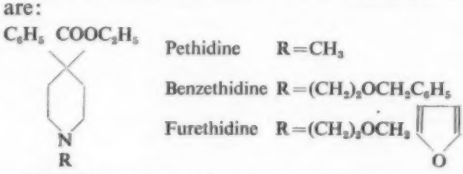
FIVE of a series of new compounds prepared by Frearson *et al.* (1960) and investigated pharmacologically by Blair and Stephenson (1960) and Lister (1960) appeared to possess major analgesic properties which merited clinical investigation. But the dearth of suitable patients for inclusion in clinical trials of major analgesics in the wards of general hospitals is a serious obstacle to those who wish to carry out such trials. The use of major analgesics for the relief of pain in general wards is not so extensive as one might suppose and when patients have to be selected for intelligence, co-operativeness and constancy of pain the number of them available for clinical trials becomes very small. (On one occasion a pilot trial conducted in a teaching hospital of over 600 beds by one of us (D.A.C.), and involving only 6 patients, took nearly 6 months to complete.) Since it was felt that suitable patients would be more readily available in a maternity hospital than in general wards, and since the new compounds are related to pethidine, the usual analgesic of choice in labour, it was decided to conduct a clinical trial with these compounds in the Leeds Maternity Hospital.

After preliminary screening for safety in healthy volunteers a pilot trial was done with the five compounds. From the information thus obtained it was decided that two of the compounds—benzethidine and furethidine—merited further examination so a full clinical trial was designed using pethidine as the standard.

The structural formulae of these compounds are:



The object of the trial was to compare, at the doses used:

(i) The analgesic effect.
(ii) The frequency of undesirable side-effects in the mother.
(iii) The frequency of desirable side-effects in the mother.
(iv) The frequency of adverse effects on the child, occurring when these three compounds are used as analgesics in labour.

METHODS

Selection of Patients

Patients were selected at an antenatal clinic at about the thirty-sixth week of pregnancy.

They were women who, so far as could be foreseen, might be expected to have a normal labour, though none was excluded on the grounds of abnormal presentation or multiple pregnancy. Pre-eclampsia was not regarded as grounds for rejection unless it was severe. No woman was included in the trial if it was judged that, due to any cause, the risk to her or the child was greater than that involved in mild pre-eclampsia or uncomplicated breech delivery. In all cases the safety of the mother and child was regarded as being of paramount importance.

Classification of Patients

Patients were classified according to age and parity to ensure that, so far as was practicable, comparisons between the effects of the three drugs were made as the result of observations made on similar groups of patients. Since the number of groups had not to be so large as to make the experiment unwieldy the following classification was adopted:

Age: (i) up to and including 34; (ii) 35 and over.

Parity: (i) para-0; (ii) para-1 to para-3 inclusive; (iii) para-4 and over.

By this classification every patient fell into one of six groups:

A — under 35 para-0.
B — under 35 para-1–3.
C — under 35 para-4 and over.
D — over 35 para-0.
E — over 35 para-1–3.
F — over 35 para-4 and over.

No classification according to complications of pregnancy or labour was attempted since this would have made the trial unmanageable.

Grouping of Patients

Comparisons of the activities of benzethidine, furethidine and pethidine were made on triads of patients. All members of a particular triad had to fall into the same one of the age and parity groups defined above. Each member of a triad received one drug only so that in each triad one patient received benzethidine, one furethidine and one pethidine. Which drug a patient received was determined by lot before the trial began. The patients were allocated to triads at the antenatal clinic and given a code number.

Identity of Drugs

Drugs were dispensed in ampoules of identical appearance, the appropriate dose of each drug being contained in a volume of 2 ml. solvent. They were kept in the labour ward and marked with a code number only. Each number corresponded with the code number marked on the patient's history sheet which she had been allocated at the antenatal clinic. When, during labour, analgesics were necessary the midwife administered the drug from the ampoule whose number corresponded with that on the history sheet. Thus the labour ward staff knew neither the identity of the drug being used nor the triad of which the patient was a member. An emergency key, however, from which the identity of any drug could be discovered, was available in the labour ward. This was in the form of a series of sealed numbered envelopes, the numbers corresponding to those on the ampoules. In this way, had it become necessary to discover the identity of the drug given to a particular patient, the identities of the remaining treatments in the trial would not have been disclosed.

Doses

The doses used were benzethidine 20 mg., furethidine 5 mg., pethidine 100 mg.

Administration

All drugs were given by subcutaneous injection at a stage in labour when, in the opinion of the person managing the labour, pethidine would normally have been given.

Antidotes

In the unlikely event of severe respiratory depression occurring, amiphenazole, bemegride or nalorphine were recommended as antidotes.

Other Drugs

Nitrous oxide and trichloroethylene were used if necessary. Otherwise no analgesic was given to patients in the trial until one hour had elapsed after administration of the test drugs. Barbi-

turates and other hypnotics were permitted but Mist. pot. brom. et chloral was used in place of "Mist. three fifteens". Times and dates of all drugs administered during the trial were recorded.

Apart from these restrictions labour was conducted in the usual way. Thus the only variation from normal procedure was that when pethidine would normally have been given one of the test drugs was given instead.

Records

Record sheets were provided on which the following information was requested.

(1) Name, age and parity of the patient.

(2) Date of last menstrual period and expected date of delivery.

(3) Any abnormalities of pregnancy.

(4) Presentation and position of foetus.

(5) Duration of all stages of labour.

(6) Method of delivery.

(7) General condition of child at birth.

(8) Interval between cutting the cord and establishment of regular respiration.

(9) Co-operativeness of mother during labour.

(10) Incidence of nausea, vomiting and other side-effects in mother.

(11) Occurrence of post-partum haemorrhage.

(12) Maternal pulse rate and blood pressure after delivery.

(13) Drugs (including inhalation anaesthetics) given during labour with times and dates.

(14) Name and status of person delivering baby.

(15) Name of person keeping record.

(16) Other observations considered relevant by labour ward staff. (Most of these details could be recorded at leisure from the case-history sheets.)

When it was decided to administer an analgesic the patient was asked to assess the severity of her pain and this was recorded according to the following code:

0=none
1=slight
2=moderate
3=severe
4=very severe.

At the same time the foetal heart rate and frequency of uterine contractions were observed and recorded. The analgesic was then administered and similar observations were made and recorded thirty minutes and one hour after injection.

Criteria

(i) *Analgesia.* The object of the trial was to select the best of the three drugs used on the basis of all their actions. The design of the trial precluded any quantitative assessment of depth or duration of analgesia produced by any of the drugs.

Analgesia was therefore regarded as an all-or-none effect. A reduction of one unit or more in the severity of pain one hour after injection constituted analgesia. Duration of labour, of course, varies greatly from patient to patient, but most patients remain in labour for one hour after injection if normal routine is followed. It was therefore thought likely that if observations were made one hour after injection, it would be possible to amass data for a useful comparison of the analgesic effects of the three drugs. A useful analgesic will have produced and retained its analgesic effect one hour after administration. Duration of analgesia could not be assessed in this trial because of variation from patient to patient in the duration of labour.

(ii) *Maternal side-effects.* These were also treated quantally. Post-partum haemorrhage was defined as the loss of 600 ml. or more of blood from the birth canal after delivery.

(iii) *Foetal side-effects.* Asphyxia neonatorum was defined as a delay of more than one minute between the cutting of the cord and the establishment of regular respiration.

Interpretation of Results

Comparisons were made between the analgesic effects of pethidine and benzethidine, pethidine and furethidine, and between benzethidine and furethidine. Similar comparisons were made concerning undesirable side-effects on the mother, desirable side-effects on the mother and undesirable side-effects on the child.

The doses of the drugs used were decided

from the information obtained in the experiments on human volunteers and the pilot trial. The doses of benzethidine and furethidine used were the largest that were considered reasonable, and from the pilot trial results it was believed that they were approximately equianalgesic with a dose of 100 mg. of pethidine. Hence if in this trial at these doses the new drugs were confirmed as equianalgesic with pethidine the decision whether they had clinical advantages over pethidine would depend on whether the evidence concerning side-effects was in their favour or not. If the results of the trial should show that the new drugs were more potent analgesics than pethidine at the doses used, then, providing the evidence about the side-effects from the new drugs was not unfavourable, they would merit introduction into clinical use. However, should the trial establish that the new drugs were less effective than pethidine as analgesics, they could be discounted at once as it was not considered advisable to give larger doses than those used in the trial.

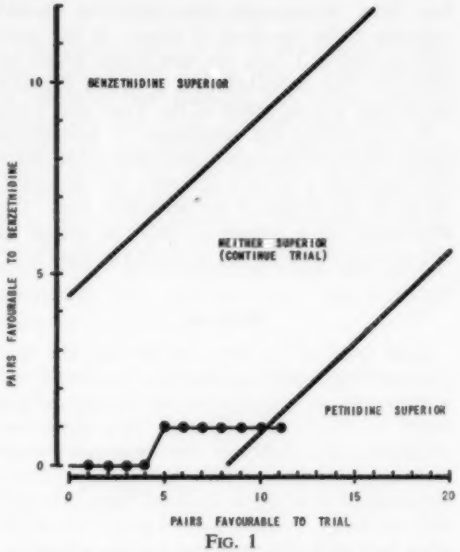


FIG. 1

Graph for comparison of analgesic effects of pethidine and benzethidine.

Analysis of Results

An experimental design using sequential analysis was used in the trial (Wald, 1947).

As the doses were supposed to be equianalgesic the odds ratio ought to be 1. An odds ratio of less than 0·625 in favour of the new drugs would mean that pethidine was a more potent analgesic at the doses used. An odds ratio greater than 1·6 in favour of the new drugs would indicate that the new drug had more analgesic effect at these doses. The probability of making a wrong decision in favour of either pethidine or a new drug was accepted at the 2 per cent level.

When equianalgesic doses are given the superiority of any drug must be measured in terms of side-effects. In this trial we had to determine whether undesirable side-effects were absent more frequently after pethidine than after the new drugs. If they occurred equally often after pethidine and the new drugs then the new drugs were to be regarded as not superior to pethidine. An odds ratio of 1·2 or less in favour of the new drugs would be taken as evidence that no improvement on pethidine

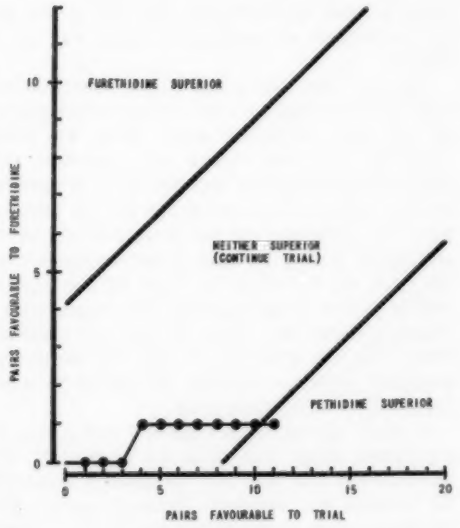


FIG. 2

Graph for comparison of analgesic effects of pethidine and furethidine.

had been found and that pethidine should continue to be the drug of choice. If the odds ratio exceeded 3 then the new drugs would be superior. The probability of a wrong decision either way was accepted at the 5 per cent level.

In comparing the incidence of side-effects due to benzethidine and furethidine odds ratios of 0·625 and 1·6 were accepted for the calculation of the slopes of the boundary lines. The probability of a wrong decision in favour of either drug was accepted at the 5 per cent level.

Results

Each triad of patients included in the trial produced three pairs of observations of analgesic activity and of side-effects, i.e., a comparison could be made between each new drug and pethidine, and between the two new drugs themselves. Not all triads, however, produced information of value to the trial. Such information was only obtained when a pair of observations indicated that one drug had an advantage over another, e.g., produced analgesia when the other did not. Figures 1–3 summarize the information gained from such pairs of observations as were favourable to the trial so far as the assessment of analgesic activity was concerned.

Figures 1 and 2 show that 20 mg. benzethidine and 5 mg. furethidine were inferior as analgesics to 100 mg. pethidine when given by subcutaneous injection. There was therefore no point in continuing the experiment to determine whether either of the test drugs had an advantage over pethidine so far as side-effects were concerned. It may be stated, however, that when the trial was curtailed the trend of the results was in favour of pethidine in this respect also. Figure 3 shows that when the trial was stopped there was no evidence of any difference in analgesic potency between benzethidine and furethidine at the doses used.

It might appear from Figures 1 and 2 that a significant result was obtained from only 33 patients but this was not the case. A total of 69 patients was necessary because some pairs of observations were not favourable to the trial and there was some wastage due to uncompleted triads.

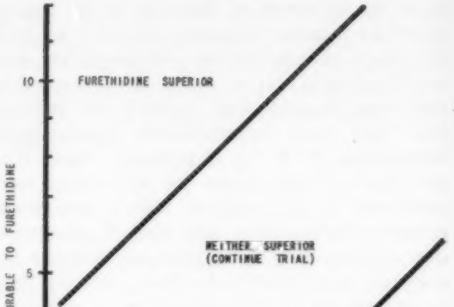


FIG. 3
Graph for comparison of analgesic effects of benzethidine and furethidine.

Taking into account all the data obtained during the trial the following results were obtained:

(i) 61 per cent of all patients receiving 100 mg. pethidine obtained analgesia.
(ii) 27 per cent of all patients receiving 20 mg. benzethidine obtained analgesia.
(iii) 33 per cent of all patients receiving 5 mg. furethidine obtained analgesia.

Discussion

Much information on the analgesic potency and the incidence of side-effects of pethidine is available so it was possible to set such limits for the sequential analysis that it could be predicted that the longest likely series of observations needed to give an answer within the set limits would not demand more patients than would be available in a reasonable period of time. On the anticipated availability of patients the longest series of observations expected from the

limits set might have taken about a year to complete. However, only 69 patients were needed to provide the answer and in fact the trial was completed within six months.

A feature of this trial was the ease with which it was carried out once the limits had been set for the sequential analysis. Most of the information required could be obtained from the case-history sheets and at no time was the double-blind technique in jeopardy. Patients were readily available and very little extra work on the part of the midwives who assisted in making the observations was involved. Significant results were rapidly obtained and we feel that this technique is very valuable in obtaining a quick and reliable clinical assessment of the activity of new analgesic drugs, especially in obstetrics. The ethical advantages of a technique which enables an investigator to discontinue the use of an inferior drug at the earliest possible moment are obvious.

ACKNOWLEDGMENTS

Our thanks are due to Sir Andrew M. Claye and Miss Ursula Lister who kindly allowed us access to their patients, and to the patients themselves for their co-operation. We are grateful to the midwives, resident staff, pupil midwives and medical students in the Leeds Maternity Hospital who helped us with the observations and records. We also wish to thank Dr. E. S. Stern of J. F. Macfarlan & Co., Edinburgh, who supplied the drugs, and Messrs. Reckitt & Sons Ltd. of Hull, who met the expenses of the investigation.

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X-RAY PELVIMETRY

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FOR many years, in Cresswell Maternity Hospital, X-ray pelvimetry has been carried out in all primigravidae and also in the multiparae who give a history of dystocia in previous labours. The films of 2,000 unselected and consecutive primigravidae have been reviewed with a view to discovering the average pelvic measurements, the incidence of contracted pelvis and the morphological pelvic types in this contracted pelvis group.

Initially only the lateral view is taken in each case and, if diminished measurements are discovered, further views of the brim or the outlet are taken, depending on the measurement, inlet or outlet, which has been noted as reduced. Generally contracted pelves which are very rare had both brim and outlet views taken and the results recorded in full.

The series was divided into social groups according to the type of bed booked by the patient for the confinement.

General. Section three: patients for whom hospital accommodation is provided free of charge.

Amenity. Section four: patients who pay a proportion of the cost of the hospital bed.

The average pelvic measurements and the incidence of contracted pelvis are compared between these social groups.

Lastly, the pubo-vertebral angle, measured between the plane of the pelvic brim and the plane of the 4th and 5th vertebral anterior surfaces, was compared in two groups of patients to determine the relationship, if any, between the angle and the station of the foetal head near term.

RESULTS

The distribution of the antero-posterior dimensions of the pelvic inlet and outlet of the 2,000 patients is shown in Table I. The average true conjugate was 11·5 cm. and the antero-

TABLE I

Distribution of Antero-Posterior Diameters of the Pelvis

	Inlet	Outlet
8·0– 8·4	1	1
8·5– 8·9	3	2
9·0– 9·4	17	9
9·5– 9·9	29	28
10·0–10·4	122	137
10·5–10·9	242	254
11·0–11·4	375	389
11·5–11·9	403	409
12·0–12·4	377	382
12·5–12·9	257	205
13·0–13·4	97	102
13·5–13·9	54	57
14·0–14·4	23	23
14·5–14·9	—	2
15·0–15·9	—	—
	2,000	2,000

Average Inlet A.P. = 11·5 cm.
Average Outlet A.P. = 11·4 cm.

posterior diameter of the outlet 11·4 cm. The majority had measurements between 10·5 cm. and 13 cm., the percentage of the total inlet measurements being 79·5 per cent and of the outlet 81·9 per cent. The smallest inlet measurement was 8·2 cm. and the smallest outlet 8·3 cm.

Those patients with an antero-posterior diameter, inlet and outlet, between 10 and 10·5 cm. are considered to be in the lower limit of normal or in the category of the slight pelvic contraction. One hundred and twenty-two inlet cases (6·1 per cent) and 137 outlet cases (6·9 per cent) occurred in this group. Measurements below 10 cm. are considered evidence of definite pelvic contraction and Table I shows that 50 cases (2·5 per cent) had a contracted inlet and 40 cases (2 per cent) had a contracted outlet. Four cases (0·2 per cent) had a generally contracted pelvis.

Where the measurements were above 13 cm. no cephalopelvic disproportion was encountered with an average size of child and in this category the inlet group numbered 174 (8·7 per cent) and the outlet group 182 (9·1 per cent).

Morphological Classification

All cases which showed evidence of contracted inlet had further X-ray examinations of the brim of the pelvis, to determine the morphological classification. Brim shape is classified into gynaecoid, platypelloid and dolichopellic by means of measuring the antero-posterior and the widest available transverse diameter and calculating the brim index which is the ratio of the antero-posterior to the transverse diameter expressed as a percentage.

Gynaecoid .. 81 per cent to 99 per cent.
Platypelloid .. 80 per cent or less.
Dolichopellic .. 100 per cent or more.

Also the posterior sagittal index is calculated by estimating the percentage ratio of the portion of the antero-posterior diameter behind the widest available transverse diameter to the transverse diameter.

Where the posterior sagittal index is less than 30 per cent the prefix "andro" is added to the above types to describe the restricted space in the posterior segment.

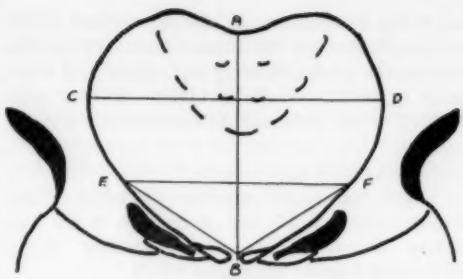

FIG. 1

The angle of the fore-pelvis.

This angle is measured by first dividing the anterior sagittal diameter A-B on the brim view film into three equal parts and at the junction of the middle and anterior thirds a line E-F is drawn parallel to the transverse diameter C-D to meet the superior pubic rami. From the points of intersection of this line with the superior pubic rami lines are drawn to the symphysis pubis and the angle E-B-F contained by these lines is the angle of the fore-pelvis.

After fore-pelvis assessment of over 100 brim pictures an angle of 114° or less was considered android.

	Brim Index	*Posterior Sagittal Index*
Androplatypelloid	80 per cent or less	30 per cent or less
Androgynaecoid	81 per cent to 99 per cent	30 per cent or less

The android shape of brim has to show a posterior sagittal index of less than 30 per cent and, in addition, an angle of the fore-pelvis of less than 114°. This type is exceedingly rare and none occurred in the present series.

As the group in Table II is selected by the discovery of a contracted true conjugate on the lateral film it does not show the general trend

TABLE II

Brim Shape in 50 Cases of Contracted True Conjugate

Androgynaecoid	7
Gynaecoid	15
Androplatypelloid	15
Platypelloid	13
Total	50

of pelvic brim shape in the population under review, but shows the predominance of the flat pelvis, the platypelloid type, among the cases with a contracted pelvic brim—56 per cent against 44 per cent with the gynaecoid brim.

Subpubic Angle

Where the antero-posterior diameter of the outlet measured 10 cm. or less an X-ray was taken to determine the subpubic angle (Chassard-Lapine technique, 1923).

TABLE III

S.P.A.	With Contracted Outlet	All Cases
65– 69	1	1
70– 74	1	9
75– 79	7	14
80– 84	5	15
85– 89	19	31
90– 94	6	5
95–100	—	1
100–104	1	2
Total ..	40	78

Average with C.P. = 83
Average all cases = 82·7

Column 1 shows the distribution of the subpubic angle among cases with a contracted outlet conjugate and column 2 the distribution of all cases in which the subpubic angle was measured radiographically:

(*a*) for reasons of contracted antero-posterior of the outlet,
(*b*) where clinical assessment suggested a narrow subpubic angle,
(*c*) where difficult low cavity forceps had occurred.

The narrowest angle recorded was 68° and the widest 120°, the latter in a patient with a generally contracted pelvis associated with congenital bilateral dislocation of the hips. The average angle in the first column is 83° with 65 per cent of them more than 85°. Over all the cases where the angle was measured the average was 82·7° and 50 per cent more than 85°.

Patients with a generally contracted pelvic brim—i.e., with an inlet and outlet antero-posterior measurement less than 10 cm. were only 4 in number (0·2 per cent), of whom 2 had a gynaecoid brim and 2 androplatypelloid.

Table IV shows the brim and posterior sagittal indices of these cases.

TABLE IV

General Contracted Pelves

Brim	Brim Index %	P.S.I. %	S.P.A.
1. Gynaecoid	87	39	80°
2. Gynaecoid	82	32	85°
3. Androplatypelloid C.D.D.	76·5	27	102°
4. Androplatypelloid ..	79	27·5	89°

Other points noted in the review were:

(1) An absence of sacral concavity in 46, in which the sacrum lay parallel to a ruler laid alongside it on the radiograph and 2 had a convex sacrum.
(2) Shallow pelves were found in 9 (3 per cent) of the 300 measured where the sacrum was less than 9 cm. in length.
(3) Congenital dislocation of the hips occurred in 2 cases, one with all measurements within normal limits and a gynaecoid brim and the other was noted among the generally contracted pelves.
(4) Spondylolisthesis, which was noted in one case, was symptomless and did not interfere with delivery.

COMPARISON OF SOCIAL GROUPS

Of the 2,000 patients under review, 1,921 were delivered in Cresswell Maternity Hospital and the remaining 79 were delivered elsewhere.

Nine hundred and sixty-five booked a "general" ward bed and 956 an "amenity" bed for their confinement. Table V shows the

TABLE V

Distribution of Antero-Posterior Diameters According to Social Groups

Cm.	Inlet		Outlet	
	General	Amenity	General	Amenity
8·0– 8·4 ..	1	0	0	1
8·5– 8·9 ..	2	1	2	0
9·0– 9·4 ..	11	6	7	2
9·5– 9·9 ..	19	10	19	9
10·0–10·4 ..	63	49	60	67
10·5–10·9 ..	125	108	130	104
11·0–11·4 ..	212	153	178	201
11·5–11·9 ..	184	209	214	185
12·0–12·4 ..	168	189	174	188
12·5–12·9 ..	104	133	100	98
13·0–13·4 ..	48	49	40	61
13·5–13·9 ..	20	34	25	32
14·0–14·4 ..	8	15	16	7
14·5–14·9 ..	0	0	0	0
15·0–15·4 ..	0	0	1	1
Total ..	965	956	965	956

"General": Average inlet 11·4 cm.; Average outlet 11·5 cm.

"Amenity": Average inlet 11·6 cm.; Average outlet 11·5 cm.

distribution of the pelvic measurements subdivided into the two social groups previously defined. In "general" patients the average measurement of the true conjugate was 11·4 cm. and the average outlet antero-posterior measurement was 11·5 cm. In "amenity" patients the average true conjugate was 11·6 cm. and the average outlet antero-posterior was 11·5 cm.

The incidence of contracted inlet, i.e., less than 10 cm., in the "general" patient was 3·4 per cent compared to 1·8 per cent in "amenity" patients and the incidence of contracted outlet was 2·9 per cent compared to 1·2 per cent.

In the category of slightly contracted pelvic inlet, between 10 and 10·5 cm., the incidence is 6·5 per cent for "general" and 5·1 per cent for "amenity" patients. Similarly for the outlet antero-posterior measurement of 10·0–10·5 cm. the percentage for both "general" and "amenity" are approximately equal, being 6·2 per cent and 7 per cent respectively.

PUBOVERTEBRAL ANGLE

This angle is measured between the plane of the pelvic brim and the plane of the 4th and 5th anterior vertebral surfaces.

In Table VI the following observations are recorded:

(*a*) Column 1: An unselected random series with the foetal head noted as engaged after the 38th week of pregnancy.

(*b*) Column 2: All cases in the series where the foetal head was free after the 38th week of pregnancy and before the onset of labour.

Between 100° and 160° the observed incidence is the same in both groups. Below 100° there are

TABLE VI

Station of Foetal Head According to Pubo-Vertebral Angle

Pubo-Vertebral Angle	Head Engaged	Head Free
85– 89	2	0
90– 99	3	6
100–109	15	9
110–119	24	22
120–129	45	62
130–139	112	112
140–149	124	121
150–159	61	67
160–169	17	6
170–179	3	1
Total	406	406

TABLE VII

Radiographic Measurement of Pelvis

	Nicholson	Ince and Young	Moir	Present Series
Obstetric conjugate	11·6	11·8	11·2	11·5
Antero-posterior of outlet	13·0	12·0	11·4	11·4

slightly more with the head engaged than those with the head free, 4·9 per cent as against 3·7 per cent, but at the other end of the scale in the range over 160° it was found that 4·9 per cent had the foetal head engaged as opposed to 1·7 per cent with the head free.

DISCUSSION

The average obstetric conjugate of 11·5 cm. obtained in this series is comparable to that obtained by Nicholson (1938), Ince and Young (1940) and Moir (1947). (Table VII.)

Maguire (1950) quotes a lower figure of 11 cm. as the average true conjugate. The population from which Nicholson (1938) and Moir (1947) drew their cases was rural and the series of Ince and Young (1940) was drawn from Metropolitan London. The population (146,000) of the present series is mainly rural, the largest town being the County town of Dumfries with a population of 30,000.

The average outlet measurement of 11·4 cm. is the same as found by Moir but less than that quoted by others. The end points stated by these three authors are the same as are used in this series.

Maguire (1950) does not give an average figure for the outlet antero-posterior but states that it varies between 9·8 and 11·5 cm. Movement of the pelvic bones and softening of the pelvic ligaments cause variation in the outlet measurement and Weinberg (1943) has shown that the increase in the outlet diameter may be from 1 to 1·5 cm. near term.

The main purpose of X-ray pelvimetry is to detect pelvic contraction and an incidence of 2·5 per cent contracted inlet and 2 per cent contracted outlet was found in this group of patients.

Generally contracted pelvis was uncommon, occurring in 4 cases (0·2 per cent), only 2 of whom were under 5 feet in height and one having bilateral congenital dislocation of the hips. In all, 3 cases of congenital abnormality affecting the pelvis were found, 2 of congenital dislocation of the hip, of whom one had pelvic measurements, and one of spondylolisthesis.

Factors Influencing Pelvic Shape

As could be expected from the mechanics concerned in pelvic development, the platypelloid type was more common among the brim contraction group.

The foetal pelvis may begin to adopt a definite morphological type during intra-uterine life, when hereditary factors control the brim shape; Kenny (1944) reported a series of 20, in which 15 female foetuses had an outline similar to that of their mothers.

According to Maguire, however, the foetal pelvis tends to be funnel-shaped.

In early childhood environment and nutrition play a significant part in determining pelvic shape, malformation being due to a deficiency of calcium and vitamin D associated with a lack of sunlight and a poorly balanced diet, notably characterized by the rachitic flat pelvis. The extreme form of rachitic flat pelvis is exceedingly rare nowadays but more minor deficiencies, causing "masked" rickets without the outward signs of malnutrition, are not revealed on external examination. These minor forms of deficiency lead to a narrowing of the obstetric conjugate and, in the present series, this is more common among the "general" patients where the incidence of contracted pelvic inlet is 3·4 per cent compared to 1·8 per cent in the "amenity" group. A proportion of this higher incidence

may be due to heredity and Baird (1949) has shown that the interchange between social groups by marriage usually cancels it out by an almost equal number of women moving from one social group to another.

In the later years of childhood the deficiency of calcium and vitamin D causes a different kind of deformity of the pelvis as the femoral heads press inwards compressing the lateral pelvic walls and producing the funnel pelvis.

Thoms (1939) and Nicholson (1943) maintain that the size and shape of the pelvis is largely dependent on the diet during adolescence and this is a reasonable hypothesis since the ossification of the pelvic bones is not complete until the 25th year of life. The stresses and strains on the pelvis would be greater during active adolescence with rapid height and weight gain than in the comparatively inactive period of the first two years of life.

Hereditary factors controlling height and physical configuration play a part in the shaping of the pelvis but the relationship between height and body configuration and shape and size of the pelvis are so variable that, although small stature and hirsutism indicate a possibility of pelvic contraction and android configuration, it is by no means possible to pick out an individual patient under 5 feet in height and state, categorically, that that particular patient must have a contracted pelvis.

Kenny (1944) has shown that an android shape of pelvis is not invariably associated with the small hirsute woman, and she describes the gynaecoid brim in a group of 40 women with a variety of external appearances.

Comparison between the pelvic size of the social groups, "general" and "amenity", shows that the average pelvic dimensions were approximately the same. The striking difference appears when we compare the incidence of contracted pelves, both of inlet and outlet, which is much more common in the "general" group. Baird (1955) suggested that the higher perinatal mortality rate among the lower social groups is due, not only to poor nutrition and low standards of living during pregnancy, but also to the higher incidence of pelvic contraction which is the legacy of the poor nutrition of the mother during early life.

Pubo-Vertebral Angle

In order to discover if the tilt of the pelvis affected the engagement of the foetal head at term, the angle between the pelvic brim and the vertebrae was measured and the results are given in Table VI. The usual method of measuring the tilt of the pelvis is by taking the angle between the pelvic brim and the horizontal but the pubo-vertebral angle gives a better indication of the relationship of the pelvis to the maternal trunk. Davies (1955) believes that man's erect posture was achieved by the extensor muscles of the back holding the trunk erect and that the pelvis maintains the quadruped relation of the horizontal. He points out that this affects the engagement of the foetal head at term, the delivery of the after-coming head in a breech delivery and the support of the uterus by the utero-sacral and transverse cervical ligaments, and if the pubo-vertebral angle is near a right angle then the foetal head would more easily engage than if the angle is obtuse and nearer 180°.

Over a range of 50° with a pubo-vertebral angle between 110° and 160° there were 366 with the foetal head engaged and 384 with the head free. Of cases with the angle below 110°, 20 had the head engaged and 15 had the head free and where the angle was more than 160°, 20 had the head engaged and 7 had the head free. Of the whole series only 406 were found with the foetal head free, which confirms that foetal head engagement can be anticipated in primigravidae after the 36th week but, considering the pubo-vertebral angle alone, without taking into account other factors, such as occipito-posterior position, the angle does not appear to have much bearing on the station of the foetal head at term.

The Sub-pubic Angle

The average sub-pubic angle of 83° in the group with contracted outlet is very close to the average angle of 84·8° for all pelves in Nicholson's (1938) series of 350 primigravidae. An angle of 80° and over is unlikely to cause difficulty in delivery of the head where the antero-posterior of the outlet is adequate, but below 80° the head cannot be accommodated

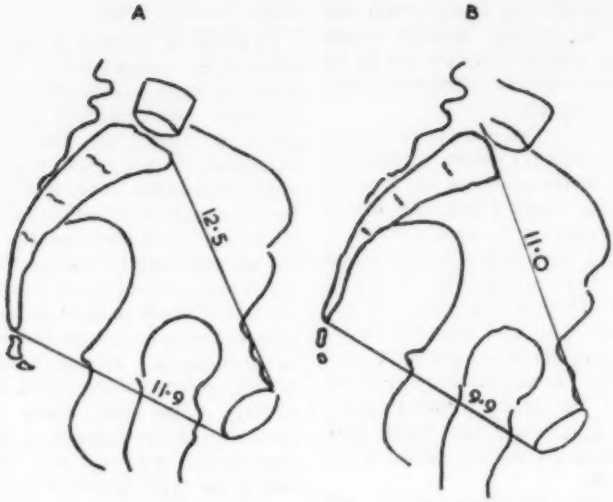

FIG. 2

closely under the pubic arch and is, therefore, thrust backwards towards the sacrum.

Where the antero-posterior diameter of the outlet is adequate, as in "A" (Fig. 2) delivery can be accomplished by episiotomy to allow the head to escape near the sacrum.

Where the antero-posterior outlet diameter is contracted as in "B" (Fig. 2) then marked dystocia would occur. The relaxation of the pelvic ligaments allows an increase of 1–1·5 cm. in the outlet diameter and may afford compensation.

SUMMARY

(1) In a series of 2,000 cases the average pelvic measurements were determined.

(2) The incidence of contracted pelvis was compared between social groups.

(3) The pubo-vertebral angle was found to have no apparent relationship to the station of the foetal head at term.

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EXPERIMENTAL CANCER OF THE UTERUS IN C_3H STRAIN MICE

BY

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CANCER induction experiments using the uterus of experimental mice as the target organ were started primarily with the object of studying the earliest recognizable cytological and histological changes in the course of uterine cancer development. It was hoped to clarify thereby the role of carcinoma *in situ* in the natural history of malignant disease. Although our results were disappointing with regard to the last mentioned specific problem, we succeeded in inducing uterine malignant tumours in a high percentage of our experimental mice and some of the tumours induced by implantation or application of carcinogens appeared interesting enough to warrant publication of our results.

METHOD

Our experiments were subdivided into three distinct groups:

Group I comprising 34 C_3H Bittner strain mice, aged between 5–7 weeks, were treated by the Murphy (1953) technique, i.e., a string with a knot impregnated with a suspension of 20-methyl-cholanthrene in wax was inserted into the cervix uteri. This was achieved at first by using a child's auroscope as a speculum and introducing the string threaded through a blunt needle into the cervix uteri under direct vision; the needle was guided blindly through one uterine horn and pushed through the abdominal wall. The string was pulled until the knot was felt to get stuck in the cervix and secured in position by tying it to the abdominal wall. This technique was later abandoned because of its technical difficulty and high mortality. After we had treated the first 17 animals in this way and lost 10 in the immediate post-operative period we used a modification of this technique for the last 17 animals in this series. A laparotomy was performed under general anaesthesia, then a blunt needle threaded with the sterile string carrying the wax-impregnated knot was introduced blindly into the cervix through the vagina and thence guided through one uterine horn under direct vision. The tying of the string to the abdominal wall was carried out in the same way as in the previous experiment. The abdomen was then closed in layers. There was very little blood loss at the time of operation and post-operative recovery was rapid. Using this modification only one animal was lost post-operatively.

Group II comprising 15 experimental animals were treated by implantation of carcinogen-impregnated string into one uterine horn; in 6 so treated animals the carcinogen-containing uterine horn was marsupialized in order to obtain direct access to the developing tumour. Of these 15 mice, 5 died post-operatively.

Group III comprising 23 experimental mice were treated by twice weekly applications of a 1 per cent 20-methyl-cholanthrene suspension in acetone to the cervix uteri. Only 1 of these animals developed cancer 7 months after the beginning of treatment. Five animals died intercurrently without evidence of tumour formation at post-mortem examination. The 17 surviving mice were subsequently treated by string insertion into the cervix 8–11 months after painting had been started.

Beginning 4 weeks after the introduction of the carcinogen each mouse was closely studied by vaginal cytology. Smears were taken twice

a week from each animal until abnormal cells appeared in the films, when smears were taken every day. Material for cytology was obtained by introducing a thin orange stick into the vagina and scraping the fornices and cervix. The cells adhering to the stick were then spread on a glass slide, fixed in a mixture of 7 parts tertiary butyl alcohol and 3 parts absolute alcohol and stained by the Papanicolaou technique (Papanicolaou *et al.*, 1943).

Anatomy and Physiology of the Genital Tract in Mice

The mouse uterus is composed of two uterine horns which join to form a long narrow tube, the cervix uteri. The upper part of this tube is covered by a single layer of high columnar epithelium and the lower by stratified squamous epithelium. Very few cervical glands are seen in the mouse uterus. The cervix reaches low down into the vagina thus creating deep vaginal fornices which are covered by squamous epithelium. When taking smears we endeavoured to collect material from these fornices.

The mouse has an oestrous cycle lasting approximately 4–6 days. In di-oestrus the smear is very cellular (Fig. 1) containing many basal cells and pre-cornified small squames which absorb the eosinophilic or the cyanophilic stains and there are usually also many leucocytes. At the height of oestrus the film is mainly composed of large clusters of keratinized cells which are anuclear and absorb the Orange G of the Papanicolaou stain and there is, normally, complete absence of leucocytes (Fig. 2). This keratinized material is broken up in the post-oestrous phase by leucocytes and mucus (Fig. 3). A little later the epithelial cells gradually re-appear in the film.

In the normal, untreated mouse the exfoliated epithelial cells are all of squamous origin and very much resemble the exfoliated cells collected from the human vagina during the menstrual cycle, except, of course, during the oestrous phase, which is specific to rodents. Columnar cells have not been found in the healthy untreated mouse but we did recover them in our experimental animals after cancer induction procedures, probably as the result of a mild endocervicitis following the operation trauma or as a reaction to the repeated scraping of the cervix with an orange stick when taking smears.

This corresponds with our experience that endocervical cells are normally absent in smears taken from the human female; when found in films they indicate the presence of cervicitis, erosion, etc. (Fig. 4).

Results

Of the 34 C_3H mice in Group I, 15 developed malignant disease, 17 died either as the result of the operation or subsequently after an outbreak of fighting in the cages. One is still alive and free from disease 20 months after the insertion of the carcinogen and 1 died of a spontaneous breast tumour.

Thirteen of the total number of tumours induced in the manner described above were squamous carcinomata, some of them keratinizing, and 1 was a fibrosarcoma. One animal developed 2 histologically distinct tumours, a fibrosarcoma and a squamous carcinoma at the same site.

These cancers developed in a remarkably short time after application of the carcinogen, the majority of them (9 out of 15) being diagnosed around 90 days after induction; the shortest interval between carcinogen administration and tumour development in this series was 43 days and the longest 198 days.

Of the 15 animals in Group II, 9 were treated by implantation of carcinogen into 1 uterine horn. Of these 9 mice 2 died post-operatively, 4 died of spontaneous breast tumours without evidence of genital tract malignancy 3 (1 case), 6 (2 cases), and 7 (1 case) months respectively after operation. One developed an anaplastic carcinoma of the uterus and one a highly cellular spindle-celled tumour invading large bowel, the histological appearances suggesting a poorly differentiated leiomyosarcoma or anaplastic fibrosarcoma. One animal is still alive and free from disease.

The remaining 6 animals in this group were treated in the same way but the uterine horn with the carcinogen implant was marsupialized. Three of these animals died post-operatively, 2 died intercurrently 6 months later and 1 is still

FIG. 1
Mouse smear: Di-oestrus.

FIG. 2
Mouse smear: Oestrus.

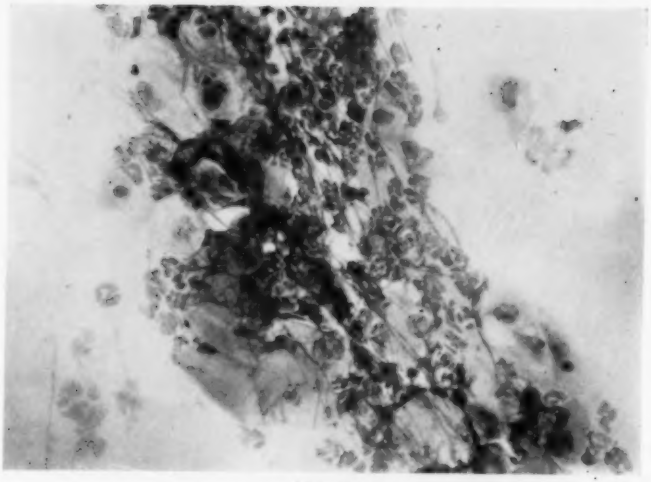

FIG. 3
Mouse smear: Post-oestrus.

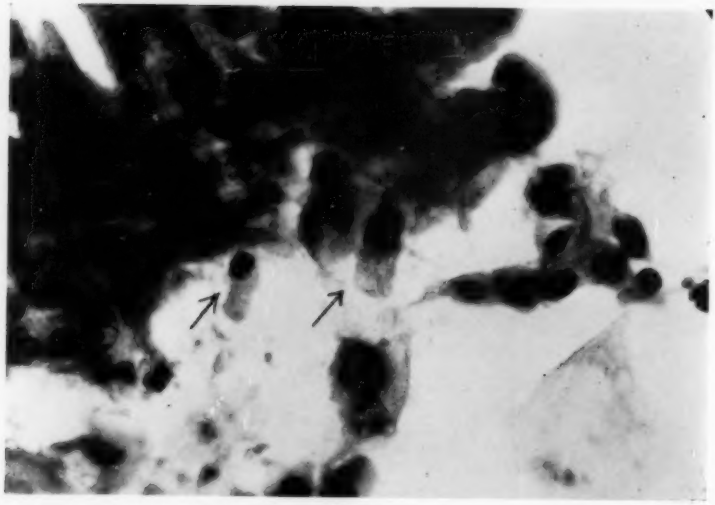

FIG. 4
Mouse smear: Endocervical cells.

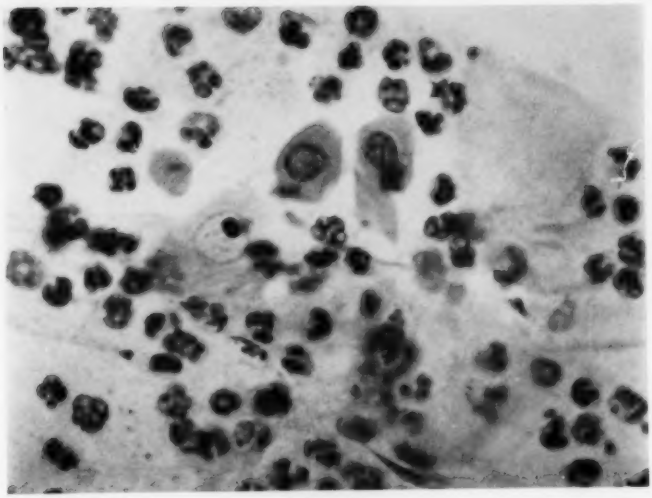

FIG. 5
Dysplastic cells.

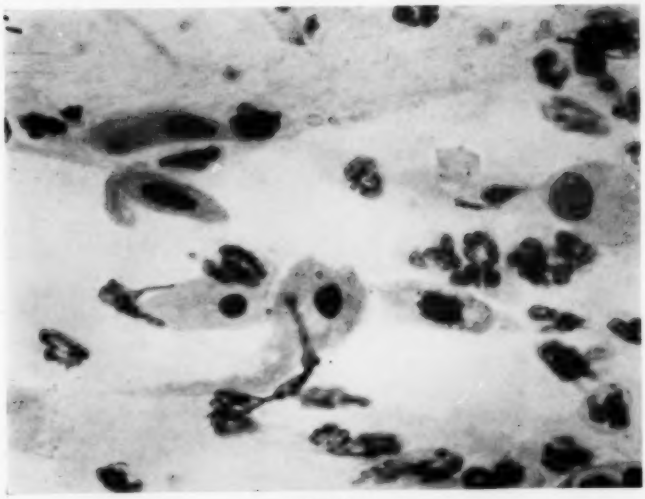

FIG. 6
Dyskaryotic cells.

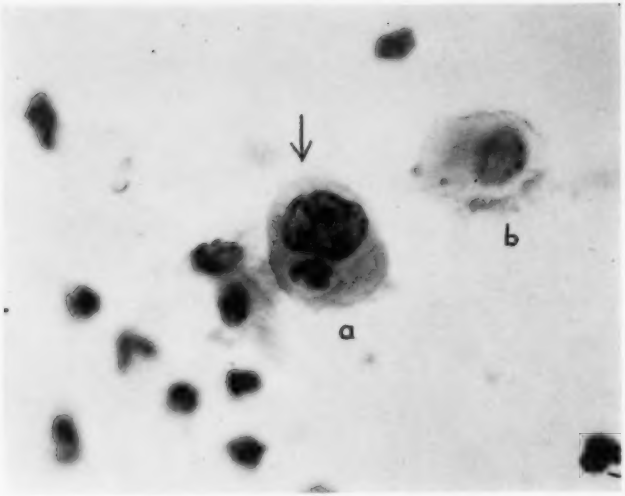

FIG. 7
(*a*) Squamous cancer cell; (*b*) dysplastic cell.

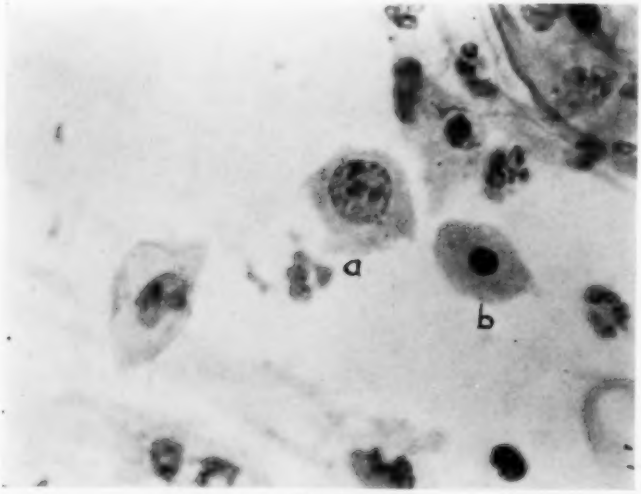

FIG. 8
(*a*) Squamous cancer cell; (*b*) dyskaryotic cell.

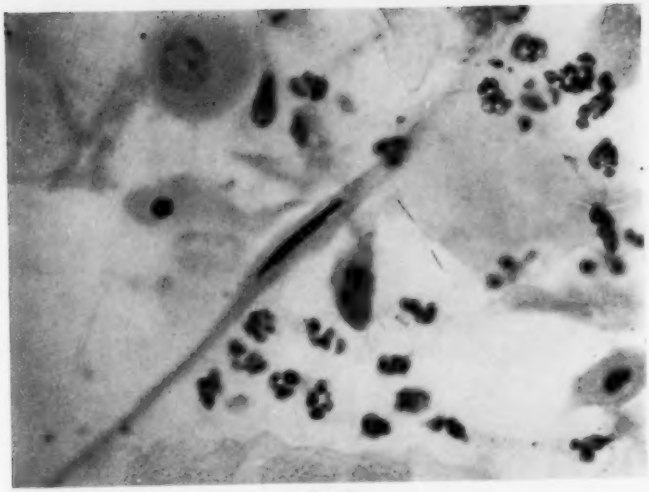

FIG. 9
Squamous cancer cells.

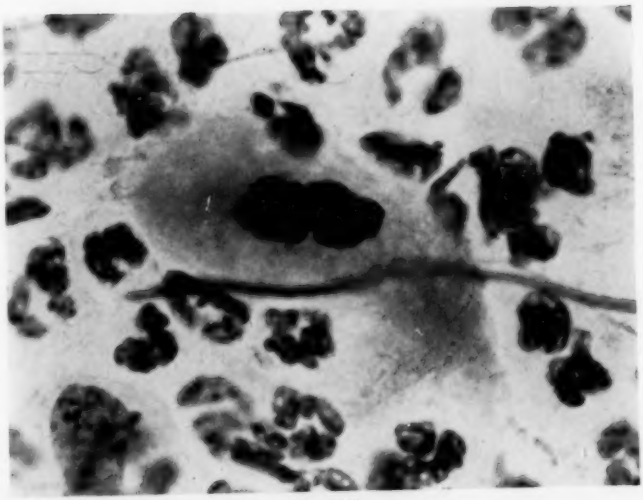

FIG. 10
Squamous cancer cells.

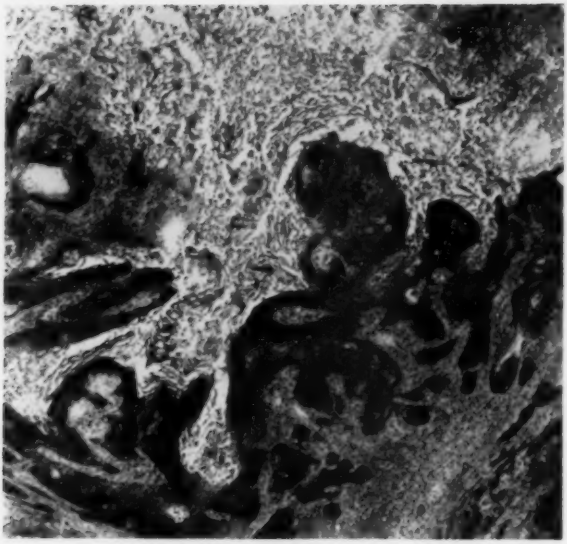

FIG. 11
Histological section: Papillomatous hyperplasia.

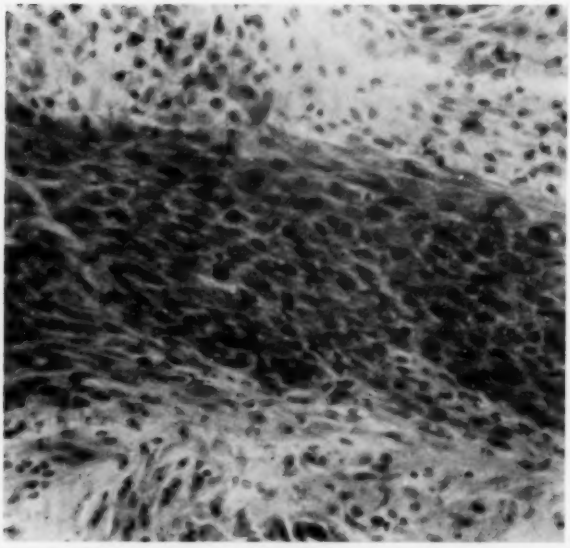

FIG. 12
Histological section: Carcinoma *in situ.*

E.W.

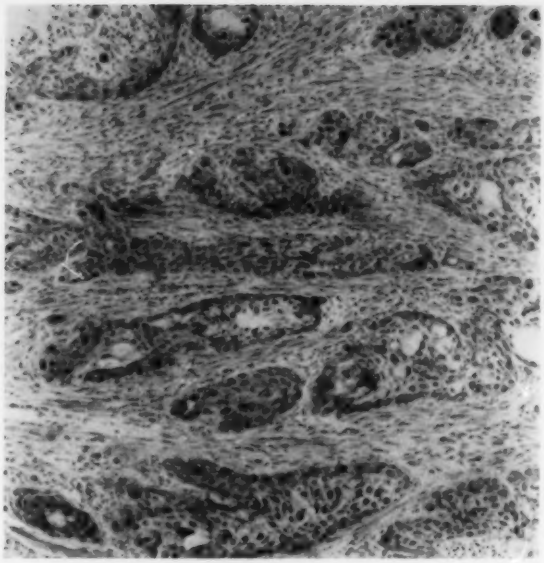

FIG. 13
Histological section: Invasive carcinoma.

FIG. 14
Histological section: Invasive carcinoma encroaching on ureters.

E.W.

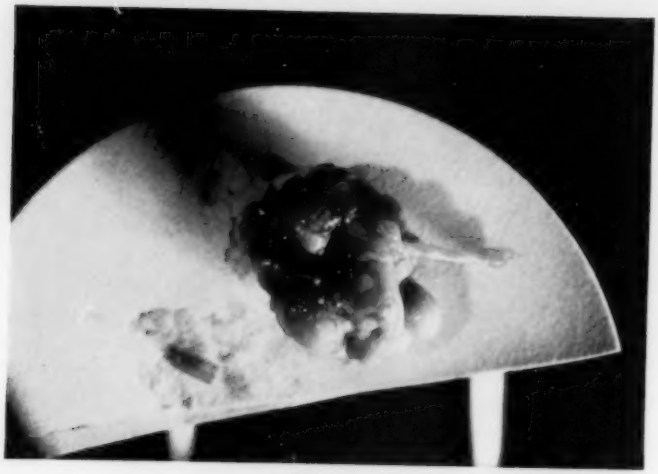

FIG. 15
Mouse tumour. Macroscopic appearances.

FIG. 16
Mouse tumour. Macroscopic appearances.

alive and free from disease. The technique of marsupialization of a uterine horn in immature mice is difficult owing to the very small size of these horns with lumina less than 1 mm. in diameter. Although we were successful in the 6 experimental animals of this group insofar as the uterine horns were marsupialized to the abdominal wall so that a thin wire could be passed through the treated horn at the end of operation, we failed to keep the marsupialized horn open for more than a few days post-operatively. We had hoped to be able to prevent closure of the horn by introducing a fine polythene tube but could not find one with a lumen narrow enough.

Of the 23 mice in Group III treated by bi-weekly painting of the cervix with carcinogen only 1 developed a cervical carcinoma 7 months after the experiment had been started. Two died intercurrently and two developed spontaneous breast tumours. The remaining surviving animals were subjected to string insertion into their cervices 7–9 months after painting had been started, but the strings were removed 3–7 days after insertion. Shorter contact of the animal with the carcinogen was desired in the hope of influencing the rate of growth (see discussion). Only one of the animals so treated developed cervical cancer 82 days after operation. Ten animals died during operation (anaesthetic death) or intercurrently and 7 are still alive and free from disease.

Discussion

Cytological study of the experimental animals by regular, at first bi-weekly and later daily, smears showed a close correlation with the histological findings. The sequence of events which led to cytological diagnosis of malignancy was the same in all squamous carcinomata observed. We allowed our first 3 tumours to grow to a respectable size in order to obtain the fullest possible insight into the progression of disease, but killed the next animals at the first appearance of atypical cells in their smears.

The first change noticed was the appearance of a general smear pattern suggesting an inflammatory reaction: i.e., excess of leucocytes, clustering of cells, slight irregularities in nuclear outline, presence of double-nucleated cells and finely granular chromatin structure (Fig. 5). We call this stage, in accordance with Professor van Haam (1955, 1956), dysplasia and the slightly abnormal epithelial elements dysplastic cells.

Three to 4 days later more markedly atypical cells made their appearance. These cells were characterized by hyperchromatic malignant-looking nuclei but did not show the typical disturbance in the nuclear-cytoplasmic ratio found in true cancer cells (Fig. 6). These cells are called *dyskaryotic* in accordance with Papanicolaou's nomenclature (1943) for equivalent cells found in vaginal smears of female patients. These cells persisted in the smears until the animals were sacrificed. Definite and unmistakable cancer cells were found a few days after the appearance of these dyskaryotic cells (Figs. 7, 8, 9, 10). The close resemblance of these malignant cells in mouse cancers to those derived from carcinoma of the cervix in women struck us as remarkable.

Figures 11, 12 and 13 are photomicrographs of histological sections of these carcinogen-induced tumours, showing the sequence of events in tumour development. Figure 11 corresponds to the cytological pattern of dysplasia and shows hyperplastic changes. Figure 12 represents the carcinoma *in situ* stage. The animal was killed 24 hours after the first appearance of dyskaryotic cells in the vaginal smear. The area shown is typical of the changes usually associated with carcinoma *in situ* but elsewhere the lesion had already penetrated the basal membrane. Figures 13 and 14 are examples of invasive cancers. Figures 15 and 16 are photographs of their macroscopic appearances. None of these tumours produced distant metastases but invasion into adjacent organs took place rapidly (Fig. 14). We were impressed not only by the short time interval between carcinogen insertion and tumour development (induction time) but also by the rapid advance of tumour growth once carcinogenesis had been initiated.

Since the aim of this investigation was mainly concerned with the study of carcinoma *in situ*, we sacrificed our next few animals at the first appearance of dyskaryotic cells in the

smears. We had hoped to correlate the cytological pattern to certain stages in the histology of the disease with the ultimate aim of finding out whether a given microscopic lesion could revert to normal spontaneously. It was hoped eventually to design a suitable biopsy instrument to obtain histological proof of cytological findings with survival of the animal. It appeared, however, that when the animals were killed 24 hours after the first appearance of dyskaryotic cells in the smears, in the absence of a palpable tumour or macroscopic abnormality, the histological appearance of the malignant growth had already surpassed the "*in-situ*" stage and early invasion had taken place. A delay of 24 hours between taking and staining of the smears, screening the films and killing the animals, seemed unavoidable. When the animals were sacrificed at the earlier "dysplastic" stage histology gave no evidence of malignant growth.

In order to decide whether this rapid development of cervical cancer could be slowed down by variation of the method of cancer induction we decreased the size of the strings and knots, using thinner material, thus reducing the actual amount of carcinogen introduced. Since this alteration in technique did not affect the speed of tumour development (in fact, while trying out this method, we observed the shortest induction time, 43 days, in this series), we decided to apply the carcinogen by painting the cervices of the next group of mice. Unfortunately only one mouse so treated developed carcinoma of the cervix 7 months after the start of the experiment and again, when the animal was killed, 24 hours after the first positive smear, the tumour was already invasive. Another approach was made by inserting the carcinogen on string for a limited period only, varying between 3 and 12 days. By placing the knot at some distance from the end of the string, the free end remains accessible from the vagina after the knot has been placed and secured in the cervix and can be easily pulled out again from below after cutting the abdominal ligature. This technique was applied to the surviving animals in Group III who had failed to develop cervical cancer after painting of their cervices with carcinogen. Only one of this group of re-treated mice developed a cervical cancer 89 days after insertion of the carcinogen which had been left *in situ* for 12 days. Tumour development, once initiated, progressed with the same rapidity as in the previous experiments. We ascribe the low "take-rate" in the last series to the fact that these animals were much older (8–10 months) than the mice in the first series of experiments (5–7 weeks).

The results of these experiments suggest that carcinogen-induced cancer of the cervix in C_3H strain mice progresses with such an explosive vehemence that a stage in its development comparable to "carcinomata *in situ*" either does not exist at all or its duration is too fleeting to be recognized.

In only 2 instances did we succeed in inducing malignant growth in the uterine horns. In neither case was it possible to recover or recognize atypical cells in vaginal smears.

Summary

(1) Squamous cancer of the cervix was induced experimentally in 17 C_3H Bittner strain mice either by insertion of a string impregnated with 20-methyl-cholanthrene into the cervix or by bi-weekly painting of the cervix with a 1 per cent suspension of 20-methyl-cholanthrene in acetone.

(2) Vaginal smears were taken at first at twice weekly and later at daily intervals and the cytological findings correlated with histological appearances.

(3) All cervical tumours exfoliated satisfactorily and were easily recognized in smears.

(4) Tumour induction, using the string method, was rapid, the average induction time being 90 days. The shortest induction time observed was 43 days and the longest 198 days.

(5) The induced tumours developed rapidly and no phase comparable to "carcinoma *in situ*" was observed.

(6) Painting of the cervix in 23 experimental animals produced only one malignant tumour 7 months after the start of the experiment. Tumour development, once initiated, was as rapid as with the string induction method. Subsequently the survivors of this experiment who had failed to develop cancer after painting

with carcinogen were re-treated by the string method. The carcinogen was left *in situ* for short periods only (3–12 days). One animal only developed a malignant growth. It is thought that the advanced age of these mice was responsible for the low take-rate.

(7) Of 13 mice, who received carcinogen impregnated string implants into 1 uterine horn, 2 developed malignant growths (1 anaplastic tumour, 1 fibrosarcoma). In neither instance were cancer cells recognized in vaginal smears. Marsupialization of the implanted horn performed with a view of obtaining direct access to the developing tumour proved unsuccessful.

Acknowledgments

My thanks are due to the British Empire Cancer Campaign without whose generous help this work would not have been possible. I am also deeply indebted to the National Institute of Cancer Research who very kindly presented me with the initial stock of C_3H strain mice. And finally I wish to thank Dr. Dan Scarpelli from the Ohio State University, Columbus, Ohio, who showed me the technique of string insertion.

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CHRONIC LOCALIZED CONSTRICTION OF THE UTERINE CAVITY IN PREGNANCY

Case Report

BY

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THE exact shape and relatively accurate size of the uterine cavity at the time of delivery of the foetus may be observed by a simple method (Torpin, 1955). This consists of filling the sac with water in a tank of water (Fig. 1). Only sacs with a small rupture are suitable but such is possible in from 25 to 50 per cent of occasions in abortions or in premature separations and at full-term deliveries, and more often if care is taken in the delivery of the placenta. The filled sac reproduces the shape and size of the uterine cavity at the time of termination of pregnancy and the usual cornual areas as well as the shape and location of the placenta as were present in the uterus. From a practical standpoint placenta praevia is probably best and most accurately identified by this procedure. It is one of the best ways to identify arcuate uterus.

In a study of a couple of thousand such sacs one and only one had the characteristics of the specimen herein reported.

In this case the sac assumed the shape of a large dumb-bell (Fig. 2). The shape differed markedly from the usual pyriform and the constriction of the membranes midway up from the site of the internal os was rather rigid and could not be effaced by manual pressure from within. This demonstrated that it was not produced by an acute constriction but must have been one that locally compressed the cavity throughout pregnancy. Furthermore the history of previous pregnancies indicates that it may be a permanent condition and may have been a factor in her two previous spontaneous abortions at or near mid-term pregnancy.

CASE REPORT

Mrs. L.S., 27 years of age, of medium constitutional type, married at 22 and became pregnant at 24. At 3-months pregnancy she spotted and then aborted 5 or 6 hours later, with apparently a normal foetus. At 26 she became pregnant again and at 4 months she began to bleed and several days later aborted an apparently normal foetus. Soon after that she again became pregnant and at the 5th month she began to bleed and after several weeks aborted by breech a normally-developed female foetus, weight 550 grams. Prior to this her laboratory report was as listed: haemoglobin, 11·0 grams; haematocrit, 35; W.B.C., 15,100; polymorphonuclears, 88; lymphocytes, 7; monocytes, 4; eosinophils, 1; urine normal; blood pressure normal. No oedema was noted.

One month after delivery pelvic examination could make out none other than a normal-shaped anteverted fundus.

One notes that the oldest haemorrhages occurred at the site of the constricted area and that the placenta lying above the ring was quite

FIG. 2
Distended inverted foetal sac hung in a tank of water. View from right side.

FIG. 3
Distended inverted foetal sac hung in a tank of water. View from left side.

normal but with some haemorrhage at its lower border.

In another interesting case the distended sac, otherwise normal, had a localized bulging, the shape of exactly one half of a 2-inch diameter balloon. This fitted over a submucous myoma expelled soon after the placenta.

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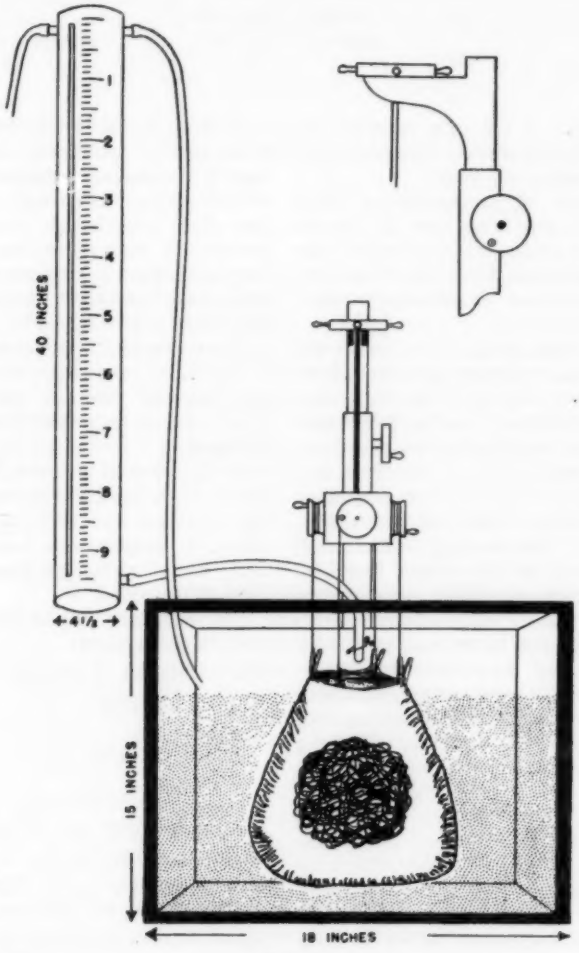

FIG. 1

Apparatus for placental sac study by fluid distension in a tank of water.

PREGNANCY WITH DIMINISHED RESPIRATORY RESERVE

BY

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"NORMAL pregnancy is not only possible but probable in the majority of cases after pneumonectomy" (Lantuéjoul *et al.*, 1956).

In the treatment of non-malignant chest disease extensive surgery is not now so frequent but there are many women of child-bearing age who had such operations when they were very popular in the treatment of pulmonary tuberculosis.

In this country there is much variation in the advice given to such women regarding child-bearing. Abroad there is possibly less restriction. Trawick *et al.*, published 1 case in 1957, where bilateral lower lobe resection for bronchiectasis was completed 9 months before conception, and Dauwe (1956) reported 2 cases of pregnancy after pneumonectomy, while the Americans, Foley *et al.* (1956), commenting on the small amount of literature on the subject, found 62 cases of lung resection in relation to pregnancy and added 2 of their own. Williams (1957) reported from Australia 18 cases of pregnancy after pneumonectomy for pulmonary tuberculosis. Of these only 2 were terminated, 1 with active tuberculous disease in the remaining lung and 1, a respiratory cripple, distressed in walking from one room to another.

In these papers little attention has been paid to the function of the remaining lung tissue, but Jeffcoate (1960), reviewing 63 therapeutic abortions includes, in the years 1954–1958, 1 for pulmonary tuberculosis and 1 for pulmonary incompetence. In this period he mentions 2 deaths from cardio-respiratory failure in pregnancy and a case of active pulmonary tuberculosis with restricted respiratory reserve and a vital capacity of 1,300 ml. who only just survived.

In Harrow, we have found it helpful to have some idea on pulmonary function from simple tests before making a decision on child-bearing. We have done tests through 1958 on women who had either considerable pulmonary damage or removal of lung tissue and had subsequently carried through a pregnancy successfully. The respiratory damage by disease or treatment had been done before 1956.

The results in 25 cases are presented (Table I).

The vital capacity, the one-second vital capacity, and the chest expansion, have been used as simple tests easily done in an out-patient department.

At the time of delivery 7 cases were under 30, 15 were aged 30–39 and 3 were over 40. The youngest was delivered at age 22 and the oldest, a woman who had 6 children before 1953, had a normal pregnancy and delivery in 1958 at the age of 45.

The procedures resulting in diminished respiratory function were:

Thoracoplasties (6 or more ribs) ..	11
Polystan plombage	2
Resections:	
Pneumonectomy	2
Lobectomy	5
Multiple segmentectomy	1
Segmentectomy in a bronchitic ..	1
Bilateral pneumothorax	2
Chronic bronchitis with long-standing pulmonary tuberculosis	1

Most of the cases treated by thoracoplasty had extensive disease and had little anti-tuberculous chemotherapy. Long periods of chemotherapy were common before the resections were done.

TABLE I

	Mean Age 1958	Mean Vital Capacity Litres	Mean Vital Capacity as Percentage of Expected	Mean 1 Second Fast Vital Capacity Litres	Mean 1 Second Fast Vital Capacity / Vital Capacity %
I. 8 cases having had unilateral collapse measures—thoracoplasty—plombage ..	38	1·7	60	1·3	78
II. 7 cases having had bilateral collapse measures or resection	30	1·7	58	1·5	81
III. 9 cases having had resection:					
(*a*) Pneumonectomy .. 2 cases..	28	1·7	55	1·4	83
(*b*) Lobectomy .. .. 5 cases..	33	2·0	67	1·6	78
(*c*) Segmentectomy .. 2 cases..	36	1·7	62	1·4	83
IV. Chronic pulmonary tuberculosis in a bronchitic .. .. .. 1 case..	45	1·7	78	0·9	59
Normal women, 8½ stone; 5 feet 4 inches ..	34	3·0	100	2·4	80

Four of the thoracoplasty cases had had a contralateral artificial pneumothorax. Three had had a pleural effusion on the thoracoplasty side. One case had open cavity drainage preceding the thoracoplasty, and another had successful diathermy excision of a basal cavity on the thoracoplasty side.

One case had pleural effusion in relation to bilateral pneumothorax and broncho-spirometry showed that oxygen uptake was almost entirely from one lung.

RESULTS

The vital capacity varied from 1,100 to 2,500 ml., a range, according to the figures of Needham *et al.* (1954), of 38 per cent to 79 per cent of the expected amount for women similar in age, height and weight. Three of the 9 resection cases gave a vital capacity of over 2,000 ml., while of the 11 thoracoplasties only 2 reached this level.

In performing these tests it was noticeable that the women tended to empty the lungs rapidly, coming suddenly to an abrupt stop. This was in direct contrast to similar tests on bronchitic men who moved larger amounts of air from their chests slowly, over a comparatively long period. Thus 4 women, 1 with a 9 rib thoracoplasty, expelled over 90 per cent of the vital capacity in the first second. The lowest figure, 59 per cent of the vital capacity expelled in the first second, was in a woman who had chronic bronchitis.

The figures of chest expansion were of little assistance, varying from ¾ inch to 2½ inches. The greatest figure was given by a woman of 31, 8 years after a left pneumonectomy and thoracoplasty.

There were 35 pregnancies in this series of 25 women.

One baby died before birth. The mother had toxaemia of pregnancy but later produced a child successfully. Another woman had a prolonged labour due to contracted pelvis; the child was not abnormal but Caesarean section was done by election in the second pregnancy. Labour was not noticeably different from normal deliveries, 4 were surgically induced, 3 having hypertension. Episiotomy was done on 3 mothers. The duration of labour extended from 1½ to 55 hours and forceps were used in 7 cases, mainly for delay in the second stage.

There was 1 post-partum haemorrhage which required a transfusion of 2 pints of blood and 1 retained placenta was removed.

There were 17 male and 17 female births. The babies were not abnormal—ranging from 2·52 kg. to 4·01 kg. with an average of 3·14 kg. Two babies of the same parents required transfusion for erythroblastosis. Sixteen were not breast fed; one mother had mastitis with each of her 2 babies.

Discussion

It has been our practice to allow these women to breast-feed the child, at least for the first 2 to 3 months, if they were willing and if breast-feeding were easily established. After this period some women appearing tired were advised to begin other feeding.

While there is no obvious bar to the number in the family, we find that more than 3 children make life troublesome for a mother with restricted pulmonary reserve and further pregnancy is not encouraged.

The number of terminations advised has been small and now we seldom recommend this procedure. It may be that in some areas termination of pregnancy is undertaken too readily for reasons of possible harm to the mother, where the risk is in fact not unreasonable.

These women do not regret having borne their own children and many are most grateful. Some women have asked to be allowed to have a child even where they knew the risk was thought high on medical grounds.

The use of simple tests of pulmonary function has been most helpful.

There has been no limit to vital capacity, 8 cases recorded 1,500 ml. or less and one woman had a figure of 1,100 ml. The ability to move air appears more important; most of these women with small vital capacity moved at least 70 per cent of their vital capacity in 1 second. It may be necessary to be more cautious at lower levels.

Therefore, in our experience in this small group of cases, with quiescent pulmonary tuberculosis, the effect of even considerable reduction in lung function on child-bearing has been less than might have been expected and termination of pregnancy is seldom advisable on this ground.

I am grateful to the obstetricians who allowed me access to their records.

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RAISED SERUM BILIRUBIN LEVELS IN ACCIDENTAL ANTE-PARTUM HAEMORRHAGE

BY

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IN estimating the plasma fibrinogen level and fibrinolytic activity in accidental ante-partum haemorrhage, it was incidentally found that the serum bilirubin level was raised before treatment and fell to normal 24 hours after delivery. It is the purpose of this paper to present 14 cases of moderate to severe accidental haemorrhage in which this phenomenon was observed.

METHOD

The blood was collected on admission before treatment (blood transfusion, fibrinogen replacement and artificial rupture of the membranes) and again 24 hours after delivery.

A dry paraffined syringe was used, with the usual precautions to prevent haemolysis and haemoconcentration and the test was performed within one hour of collection.

The estimation of serum bilirubin was done according to the method described by King and Wootton (1956). As controls, the same estimation was performed on blood specimens from 67 patients, ranging from those with normal pregnancy and delivery to those with abnormal pregnancy such as mild accidental ante-partum haemorrhage, placenta praevia, mild and severe pre-eclampsia and eclampsia.

RESULTS

Table I shows that accidental ante-partum haemorrhage of moderate to severe degree caused a statistically significant rise of the serum

TABLE I

Ante-partum and Post-partum Bilirubin Levels in Accidental Haemorrhage and Control Groups

Groups	No. of Cases	Serum Bilirubin (mg.%)	
		Ante-partum Mean ± S.E.	Post-partum Mean ± S.E.
Ante-partum haemorrhage:			
(*a*) Severe and moderate	14	1·26 ± 0·096	0·31 ± 0·036
(*b*) Mild	7	0·40 ± 0·081	0·26 ± 0·053
Normal delivery	22	0·40 ± 0·029	0·40 ± 0·023
Placenta praevia	8	0·40 ± 0·060	0·30 ± 0·053
Mild pre-eclampsia	19	0·30 ± 0·037	0·30 ± 0·030
Severe pre-eclampsia and eclampsia	11	0·40 ± 0·055	0·45 ± 0·068

bilirubin level which fell to normal 24 hours after delivery. The increase was about 3 times higher than in the control groups.

Table II shows the clinical and laboratory findings of 14 cases of accidental ante-partum haemorrhage with raised serum bilirubin level. The highest serum bilirubin level obtained in this series was 2·1 mg. per cent, which is still insufficient to produce clinical jaundice. On admission, all 14 cases had inaudible foetal heart and showed evidence of increased uterine tonicity and varying degrees of tenderness. All of them were of mixed type of accidental haemorrhage and with the exception of 3 cases there was more concealed than revealed blood loss. Eight cases were admitted with evidence of clinical shock but their raised serum bilirubin levels were not higher than those free from shock. In all cases, the Maw thrombin test showed failure of the blood to clot (11 of them had afibrinogenaemia and 3 hypofibrinogenaemia). The extent of increased serum bilirubin levels in the series was unrelated to age (youngest 27 and oldest 41), parity (all multiparous, with 8 over para-5), the presence of toxaemia of pregnancy, or the duration of bleeding as determined by the onset of revealed vaginal bleeding or abdominal pain whichever occurring first (4 to 16 hours).

Of 14 cases in this series, 13 were given blood transfusion, parenteral fluid and fibrinogen replacement. However, the amount of blood given was not enough to replace the actual blood loss because of difficulty in obtaining blood. Artificial rupture of membranes was the standard treatment in all cases, and subsequent deliveries were spontaneous except Case 4 which required Caesarean hysterectomy due to uterine inertia and increased concealed haemorrhage. All foetuses were stillborn, one was macerated. The post-partum serum bilirubin levels were unaffected by the amount of blood transfused or fibrinogen given. There was no maternal death.

Discussion

The most likely explanation of increase of serum bilirubin level in moderate and severe accidental ante-partum haemorrhage is absorption of the retroplacental blood through the placental site. The absorption is probably enhanced by increase of intra-uterine tension as indicated by increase of uterine tonicity and rhythmic contractions of the uterus during labour. Bromberg *et al.* (1957), in their investigation of foetal blood in retroplacental haematoma, suggested that in the third stage of normal labour some absorption of retroplacental haematoma took place. Furthermore, they reported a case of accidental ante-partum haemorrhage in which they found an unusually high level of foetal haemoglobin in the maternal circulation. The presence of Couvelaire uterus with haemorrhage in the uterine wall may be an additional factor contributing to the phenomenon as shown by the only case which required abdominal operation (Case 4). Nevertheless, the rapidity of the return of serum bilirubin to the normal level 24 hours after delivery suggests that the absorption of blood *via* the placental site probably plays a more important role.

The relation between the degree of elevated serum bilirubin level and the amount of blood loss in accidental ante-partum haemorrhage is difficult to assess. For instance, if there is no clinical shock, the amount of revealed vaginal blood loss before admission depends upon the patient's estimation. Although the amount of blood loss after admission can be measured, it is still only approximate due to spilling and mixing with liquor amnii. The fact that the foetuses were all dead on admission suggests that, irrespective of the amount of external bleeding or absence of shock, the degree of separation of placenta was extensive. While the size of placental compression after delivery may indicate the extent of retroplacental haematoma, placental compression may be absent if the separation of placenta is rapid and extensive as shown in Case 4. Also, the level of serum bilirubin obtained on admission may or may not represent the peak level in each individual case. Serial estimation should be more useful, but it was not practical to do so because in most cases urgent blood transfusion was required after which further estimation would give confusing results.

Summary

Moderate and severe accidental ante-partum

TABLE II

Summary of Clinical and Laboratory Findings in Moderate and Severe Accidental Ante-partum Haemorrhage

Case No.	Clinical Conditions*				Laboratory Findings			Treatment			Results				Remarks
	Duration of Symptoms (hours)	Clinical Shock	Toxaemia of Pregnancy	Onset of Labour	Plasma Fibrinogen (mg.%)	Serum Bilirubin (mg.%) Ante-partum	Serum Bilirubin (mg.%) Post-partum	Blood Transfusion (pint)	Fibrinogen (g.)	ARM	Placental Compression (area)	Blood Loss (ml.) Revealed	Blood Loss (ml.) Concealed	Child (g.)	
1 ..	7	+	−	+	0	1·25	0·30	2	1	+	2/3	[illegible]	1,300	3,750 macerated	
2 ..	4	+	−	+	0	1·10	0·20	3	2	+	1/4	1,600	450	2,500 S.B.	
3 ..	4	+	−	+	0	1·00	0·55	2	4	+	1/2	300	780	1,956 S.B.	
4 ..	5	−	+	−	0	1·10	0·30	8	6	+	nil	1,000	2,150	1,115 S.B.	Caesarean hysterectomy done 7 hours after ARM
5 ..	8	+	+	+	35	2·10	0·50	3	3	+	1/4	200	2,200	3,200 S.B.	
6 ..	12	+	−	+	0	1·60	0·25	4	6	+	1/4	100	2,000	3,117 S.B.	
7 ..	12	−	+	+	0	1·15	0·50	1	5	+	3/4	420	1,180	2,580 S.B.	
8 ..	5	+	−	+	0	1·25	0·25	2	5	+	1/4	500	1,070	2,800 S.B.	A mild attack of vaginal bleeding 12 days previously.
9 ..	16	−	−	+	0	1·25	0·40	2	5	+	5/6	550	1,270	3,190 S.B.	
10 ..	12	−	−	+	0	1·15	0·35	1	2	+	9/10	300	660	2,000 S.B.	
11 ..	5	+	−	+	142	0·75	0·15	1	4	+	4/5	700	650	2,600 S.B.	
12 ..	5	−	−	+	0	1·20	0·10	0	6	+	2/3	500	1,100	2,500 S.B.	
13 ..	12	+	−	+	0	1·15	0·35	2	6	+	2/5	800	500	3,200 S.B.	
14 ..	6	−	−	+	83	1·70	0·20	2	8	+	9/10	500	1,860	3,600 S.B.	

* Clinical conditions when blood specimens were taken. S.B.=stillborn. ARM=artificial rupture of membranes.

haemorrhage was found to be associated with an increase in serum bilirubin level which was three times higher when compared with the control groups. This increase of serum bilirubin level was not sufficient to give rise to clinical jaundice. It rapidly returned to normal level 24 hours after delivery.

We are grateful to Professor Daphne Chun for advice and encouragement.

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POTASSIUM PERMANGANATE INDUCED VAGINAL BLEEDING

BY

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SINCE the publication of the first paper on the use of potassium permanganate as an abortifacient by Lacassagne and Friess in 1932 there has been a steadily increasing flow of publications on this subject particularly in the last decade. Up to the end of 1959 some 650 cases have been described in 20 different papers in the English literature. Among the 650 cases there were 120 where the patient thought she was pregnant when in fact she was not. Abortion was successfully induced in only 31 (6 per cent) of the remainder. There have been 3 fatal cases described and a number of serious late complications. In addition 257 patients (40 per cent) required blood transfusion, an indication of the seriousness of the risk which the patient runs.

Although the practice of introducing potassium permanganate into the vagina, usually in the hope of terminating an unwanted pregnancy, originated in Europe, the majority of recent reports have come from America. Only 2 (Miller, 1951; Alment and Nicol, 1953) have appeared in the British literature but from the published correspondence which followed these communications it would seem that the practice is still quite common in this country. That this may be so is borne out by recent personal experience in South-East London. The purpose

TABLE I

Mortality and Morbidity Associated with the Intravaginal Administration of Potassium Permanganate

Author	Year	Cases
Jetter and Hunter	1949	One case of fatal $KMnO_4$ poisoning following a vaginal douche with a concentrated solution.
Wanamaker	1955	Two cases of fatal haemorrhage and shock.
McDonough	1945	One case of scarring of the posterior lip of the cervix necessitating Caesarean section for obstructed labour.
O'Donnell	1954	One case of vesico-vaginal fistula.
Henderson and Watt	1951	Three cases of scarring of the vaginal vault necessitating Caesarean section.
Kobak and Wishnick	1955	One case of pelvic peritonitis leading to intestinal obstruction.
St. Romain and Nix	1955	Four cases of scarring and stenosis of the vagina.
Webster and Steward	1957	Ten cases of scarring of the vaginal vault necessitating Caesarean section.

of the present paper is to draw attention to the clinical features of the condition and to underline its dangers. (Table I.)

Clinical Material

Three cases of vaginal bleeding induced by potassium permanganate have been seen by the author in the last three years and a further 7 cases have occurred in two general hospitals in the locality. The details of the cases are summarized in Table II. The patients' ages ranged from 17 to 36 years, 7 were married and multiparous, 3 were unmarried and nulliparous. Amenorrhoea was a feature in all the eight cases where the chemical was intended to produce an abortion but 2 of these were not in fact pregnant. The duration of pregnancy in the 6 patients who were pregnant ranged from 6 to 20 weeks. No cases of bleeding in late pregnancy from this cause have been encountered although this has been described (Webster and Steward, 1957). Of the remaining 2 patients who did not set out to induce an abortion, one inserted a tablet of potassium permanganate into the vagina as a contraceptive measure, whilst the other used a tampon soaked in potassium permanganate solution as a treatment for menorrhagia. In all 10 cases a history of having introduced the chemical into the vagina was eventually obtained. There was no case in this series where the patient douched herself with potassium permanganate solution, although this method is not uncommon in the recorded cases. The method of production of bleeding is the same whatever the mode of administration. In the case of the douche, undissolved particles of potassium permanganate are deposited in the vagina and erode the mucous membrane in the same way as do the actual tablets themselves.

Table II

Case No.	Duration of Pregnancy	No. of $KMnO_4$ Tablets Used	Treatment Employed			If Transfused	Remarks
			Expectant	Pack	Suture		
1	Not pregnant	1	✓	—	—	No	5-weeks amenorrhoea, not pregnant.
2	8 weeks	2	—	✓	✓	Yes	Very shocked on admission.
3	Not pregnant	–	—	✓	✓	Yes	Used Tampon soaked in $KMnO_4$ as treatment for menorrhagia.
4	Not pregnant	1	✓	—	—	No	Tablet used as contraceptive.
5	9 weeks	6	—	✓	✓	Yes	
6	12 weeks	?	—	✓	—	No	
7	12 weeks	8	—	✓	—	No	
8	20 weeks	6	—	—	✓	No	Ulcers on labia as well as in vagina.
9	10 weeks	2	—	✓	—	Yes	
10	8 weeks	4	✓	—	—	Yes	

Case Histories

The case histories of Cases 1 and 2 are typical and are described in more detail below.

Case 1

Miss L., aged 17 years and nulliparous, was admitted to hospital with a history of 6-weeks amenorrhoea followed by severe vaginal bleeding which started four hours after the insertion of a single 5 grain tablet of potassium permanganate into the vagina. The estimated blood loss was 2 pints (1,100 ml.).

The periods were normally subject to some irregularity but the delayed appearance of the period in this particular instance was associated with the fear of a possible pregnancy. The patient had therefore followed the gratuitous advice of a workmate and used the tablet of potassium permanganate to "bring on a miscarriage".

On examination the patient was pale but not shocked. The vagina was filled with blood clot which when removed revealed a circular ulcer in the left vaginal fornix extending on to the side of the cervix. The edges of the ulcer were charred and particles of black manganese dioxide were present in the vagina. Active bleeding had ceased and treatment was confined to irrigating the vagina thoroughly with sterile water. There was no evidence of pregnancy. The patient was discharged five days later and when seen in the follow-up clinic six weeks after discharge the ulcer had completely healed without scarring. The patient had meanwhile had a normal period.

Case 2

Mrs. S., aged 28 and a gravida-2, was admitted to hospital with a history of severe vaginal bleeding six hours after the insertion of two tablets of potassium permanganate into the vagina. She was 8-weeks pregnant and had used the tablets on the advice of a friend in the hope of inducing an abortion. The estimated blood loss was 3 pints (1,650 ml.).

On examination the patient was pale and shocked and there was active vaginal bleeding. After resuscitation and blood transfusion (4 pints, 2,200 ml.) an examination under anaesthesia was performed. This revealed a normal 8-weeks uterine pregnancy and two ulcers on the anterior and posterior walls of the upper vagina. The ulcers were deep and had well-defined blackened edges. Arterial bleeding was occurring from a small vessel in the base of the posterior ulcer. The vagina was washed out and the bleeding controlled by means of catgut sutures and a vaginal pack. The pack was removed 36 hours later and no further bleeding occurred. The patient was discharged after four days and subsequently attended the antenatal clinic. The ulcers healed without scarring and the patient delivered spontaneously at term. The child was normal.

Treatment

Five of the patients were shocked and required blood transfusion. In three the bleeding had stopped by the time the patient was admitted to hospital and local treatment was limited to irrigation of the vagina with water to wash away any remaining particles of the tablet. A vaginal pack was used to control the bleeding in 4 cases, whilst in the remaining 3 cases transfixion sutures were necessary to stop active arterial bleeding.

Results of Treatment

All of the patients made an uneventful recovery and there was no evidence of untoward late effects. All were seen six weeks after discharge from hospital, by which time the ulcers had healed completely. Four of the 6 pregnant patients were followed up in the antenatal clinic of the hospitals concerned and delivered normally of healthy offspring. The remaining 2 declined to attend the hospital antenatal clinic, preferring to make their own arrangements for delivery.

Discussion

The continued reputation which potassium permanganate enjoys as an abortifacient, in spite of the rarity with which it actually achieves its purpose, is undoubtedly due to the prompt vaginal bleeding following its use. The patient ascribes the bleeding to impending abortion, and her medical attendant is not infrequently similarly deceived. None of the 65 cases described by McDonough (1945) had been correctly diagnosed prior to admission to hospital. The classical clinical picture illustrated by Case 2 above was well described by Shull (1941) in the first account of the condition to appear in English. He drew attention to a diagnostic triad, i.e., a profuse painless vaginal bleeding in early pregnancy, associated with a tightly closed cervix and with a circumscribed charred ulcer visualized on speculum examination. In differentiating threatened abortion and potassium permanganate induced bleeding the amount of bleeding and the absence of abdominal pain should call the latter possibility to mind. A careful speculum examination enables the diagnosis to be made with certainty. Where bleeding is heavy it may only be possible to do this in the operating theatre with the patient anaesthetized. A well-defined ulcer in the vaginal or cervical mucosa with a charred

edge and often with a "mirror" lesion on the opposing vaginal wall, together with a closed external cervical os and the absence of uterine bleeding, confirm the diagnosis.

From the standpoint of treatment many patients will require resuscitation before local measures can be instituted. Once the patient's general condition is satisfactory it is very important to wash out any remaining particles of potassium permanganate by liberal irrigation of the vagina with sterile water (Webster and Steward, 1957). Failure to do this may lead to scarring and fibrosis in the vagina which often carries serious consequences to the patient's subsequent obstetric history. In many patients bleeding will have stopped by the time the patient is admitted to hospital and treatment can then be confined to irrigation. Where bleeding continues a transfixion suture provides the best way of stopping it. Generalized oozing of blood from the ulcer base can be dealt with by means of a gauze vaginal pack. This may be combined with a local application of oxycel gauze (Borrow and Friedman, 1952). The pack is removed after 24 hours and the patient can usually be discharged from hospital after four or five days. She should, however, be instructed to return immediately should any fresh bleeding occur. Secondary haemorrhage is rare but has been described (Lindsay and Ward, 1954). A follow-up of the patient is desirable to detect late fibrosis of the vagina and those patients who are pregnant need careful antenatal supervision and support since further attempts to induce abortion by other means may be made.

Summary and Conclusions

Ten cases of vaginal bleeding induced by the introduction of potassium permanganate into the vagina are described. The comparative frequency of the occurrence is emphasized and the clinical features reviewed. Attention is drawn to the diagnostic triad of painless profuse bleeding in early pregnancy in association with a circumscribed, charred vaginal lesion and a tightly-closed cervix.

None of the cases described, who were pregnant, aborted, underlining the ineffectiveness of this substance as an abortifacient.

The methods of treatment are described and the American and British literature briefly summarized.

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A SERTOLI CELL HAMARTOMA OF THE OVARY IN A WOMAN WITH CONGENITAL ABSENCE OF THE UTERUS

A Case Report

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TEILUM (1949) collected 10 cases of Sertoli cell tumours of the ovary from the literature. Wang (1955) reported that the number had increased to 16 including his own.

Such lesions associated with congenital absence of the uterus are rarer still and of some aetiological importance.

CASE REPORT

Mrs. K.J., aged 58 years. Ref. No. D.974.

Previous History

At the age of 18 years she had "osteomyelitis" of the jaw following a dental extraction. In 1954 a left local mastectomy was performed. Histological examination revealed extensive duct papillomata: there was no evidence of malignancy. In 1956 she had a laparotomy for pancreatitis. A few months later she attended the Medical Out-Patients complaining of palpitations. She was found to be suffering from a basic anxiety state. A small mass was palpable in the right iliac fossa. This was shown radiologically to be unassociated with the alimentary tract and to lie medial to the ascending colon.

In October, 1956 at laparotomy a tumour was removed from the site of the right ovary. The surgeon (R.T.) was unable to find a uterus or left appendage. She made an uneventful recovery and was referred to the Gynaecological Department.

Gynaecological History

She was the only child from an upper middle-class family, happily married, interested in clothes and housework and there was no indication of masculine tendencies. Despite treatment in her youth she had never menstruated. At first she had been worried by the amenorrhoea, but soon became resigned that "she was not as other women". She married her first cousin at the age of 29 (the son of her mother's sister) who she says is "colour blind". Sex life had apparently been satisfactory and she experienced orgasms occasionally. The marriage was sterile and she adopted a daughter now aged 31. There was no history of hot flushes or the need to shave.

On Examination

Weight, 150 pounds (68 kg.); height 5 feet 7 inches (170·2 cm.); size of shoes, 6; pulse, 100 per minute; temperature, 97·6° F. (36·4° C.); blood pressure, 160/110; average build.

She was an intelligent middle-aged woman of normal appearance with a feminine voice and no abnormal facial hair. The thyroid was just palpable. The body hair distribution was scanty. There was a left local mastectomy scar. The right breast was of normal size, shape and consistency for a woman of her age. Examination of heart, lungs, abdomen and nervous system showed no significant abnormality.

Pelvic Examination under General Anaesthesia

The pubic hair was normally distributed but scanty and the vulva was healthy. The clitoris was of normal

size. The vaginal walls were healthy and there was no discharge present. The vagina measured 2½ inches (6·35 cm.) and took 2 fingers; the vaginal vault was smooth. There was no evidence of a cervix or cervical canal. No uterus or appendages could be felt on bimanual examination.

Laboratory Investigations

Haemoglobin, 114 per cent (16·9 g./100 ml.); red blood corpuscles, 5,310,000/c.mm.; packed cell volume 48 per cent; white blood corpuscles, 10,300/c.mm.; blood group O Rh. positive; Wassermann reaction—negative.

Erythrocyte sedimentation rate: 18 mm. (Westergren) in the first hour.

Specimens of urine were collected over a period of 48 hours in December, 1957, 14 months after laparotomy. Analysis gave the following results:

Pregnanediol (Sommerville *et al.*, 1948): 4 mg. (normal maximum 6 mg.) per 24 hours.

Gonadotrophins (Lorraine and Brown, 1956a, b): 16 mg. per 24 hours (normal, 5–25 mg.).

Neutral 17-ketosteroids (Norymberski *et al.*, 1953): 6 mg. per 24 hours (normal for a woman 50–60 years, 3–10 mg.).

The patient was tested with Ishihara's Colour Cards for colour blindness. She was shown to have the Deuteranopic type of dichromatic vision, or so called "green colour blindness".

In order to establish the chromosomal sex, blood smears, skin biopsy and the tumour were examined by Mr. Dixon and Dr. Torr at the Department of Anatomy, Manchester University. They also examined oral smears (Dixon and Torr, 1956). They found all the material to have female characteristics.

Pathological Report

The tumour removed at laparotomy consisted of brownish tissue with a small thin-walled cyst, and measured overall 4·5 cm. The cyst contained thin fluid. There was considerable haemorrhage in the tissues. No yellow streaking was seen. Histological examination shows a gonad mainly replaced by Sertoli cells and interstitial cells (Fig. 1). The Sertoli cells are arranged in cords some of which have a single layer of centrifugally placed nuclei and an apparent lumen running down the centre of each cord of cells, but the cell margins are difficult to define (Fig. 3). Other cords, the larger proportion, consist of solid cylinders of cells in which the nuclei are not necessarily situated at the periphery of the cell groups and are sometimes distributed evenly over the cross-section. There are a few fine sudanophil droplets mainly in the cytoplasm of the more differentiated cords. The interstitial cells are polyhedral and eosinophilic with granular cytoplasm. They stain faintly but evenly with Sudan IV and give a positive reaction with Vines stain (Zinsser and Zinsser, 1951). They also contain granules which in some cells are positive with the periodic acid Schiff reaction and in many cells stain with phosphotungstic acid haemotoxylin. There are brown pigment granules in many cells but no Reineke Crystals can be seen. The cytoplasm of the cells stains a diffuse dull red with Massons Trichrome.

The Sertoli cell groups and interstitial cells lie, in some areas singly, intermingled or against the background of stroma or of connective tissue; or elsewhere in great groups composed of one cell type or the other (Fig. 2). The masses of interstitial cells show degenerative changes in some areas. Stroma consisting of compact spindle cell connective tissue such as is found in the ovarian cortex can be recognized occasionally but there are no ova or follicles to be seen in it. No developed testicular tubules are present. The majority of the supporting tissue is not composed of compact spindle cells but of loosely woven fibrocytes or of fine fibrillary open woven connective tissue. The organ has a fairly well defined border but little evidence of a capsule. There is no mature Fallopian tube in the sections, but the gonad is attached to muscle and to fibrous tissue in which there are a few small cystic spaces lined by a simple low columnar or cuboidal epithelium. The appearances are those of a Sertoli cell hamartoma of the ovary.

Discussion

Robert Meyer regarded Sertoli cell tumours as arrhenoblastomas which failed to produce virilizing hormone because they were well differentiated. He considered that arrhenoblastomas arose from male anlage dormant in all ovaries.

Teilum (1951) designated the androblastoma group of tumours as identical tumours of the ovary and testis with origin from potentially male cells irrespective of the qualitative hormone producing properties. The tendency to tubule

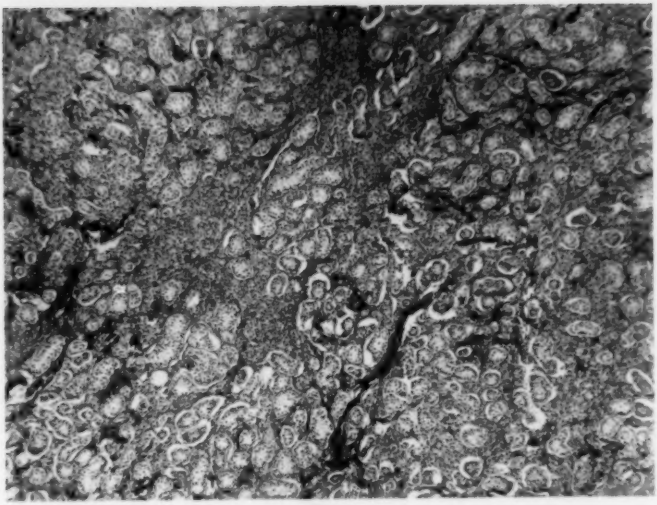


FIG. 1

General low power view of the Sertoli cell hamartoma. H. & E. ×50.

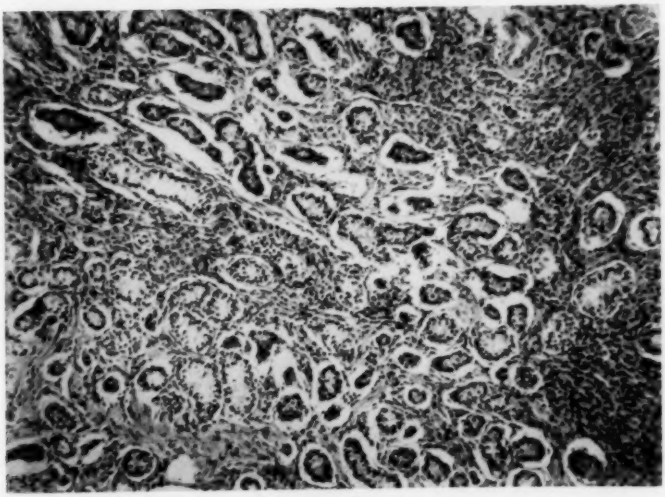


FIG. 2

View showing general arrangement of Sertoli cell cords and interstitial cells. H. & E. ×87.

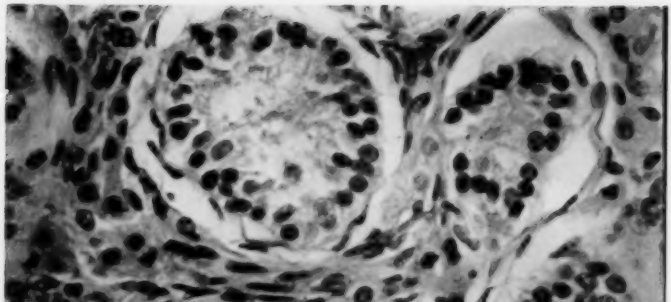


FIG. 3

Five cords of Sertoli cells cut in cross section, some of which illustrate the apparent lumen running down the centre of each cord and the difficulty in defining the borders of each individual Sertoli cell. Van Gieson. ×420.

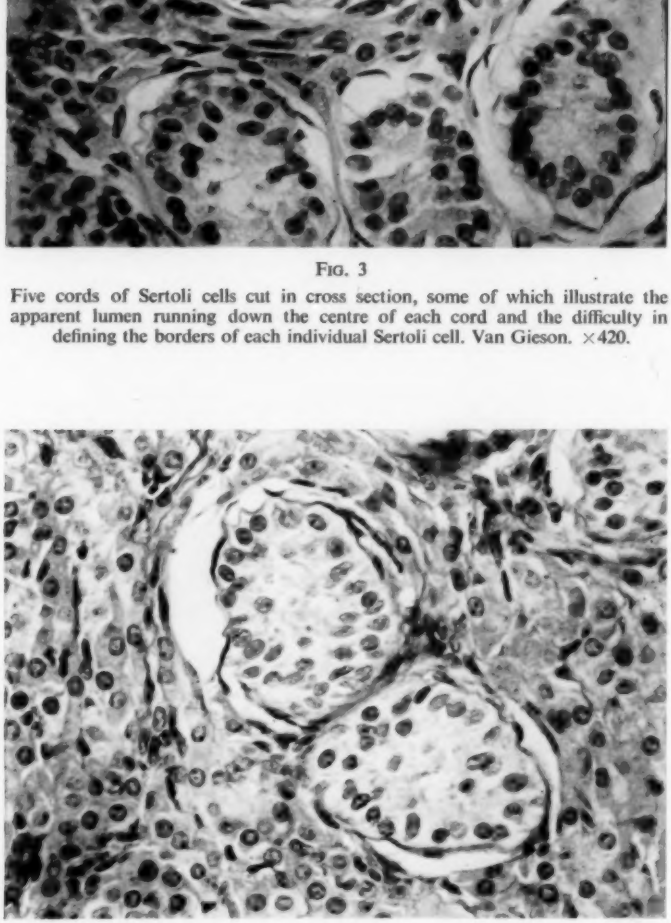


FIG. 4

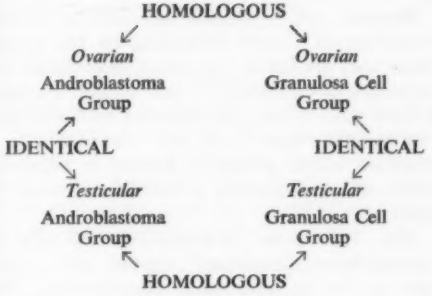
Cords of Sertoli cells surrounded by interstitial cells. H. & E. ×450.

arrangement represents efforts to reflect the normal testicular architecture. The androblastoma group consists of tumours, more or less differentiated, in which varying proportions of Sertoli and interstitial cells occur. The Sertoli cells may produce feminizing hormones and the interstitial cells virilizing hormones. These tumours therefore only produce noticeable changes in the female when sufficient male hormone is produced to bring about noticeable virilizing effects or sufficient oestrogen to cause puberty praecox, menorrhagia or postmenopausal bleeding.

Teilum (1958) recognizes an embryological homology between granulosa and Sertoli cells on the one hand and theca and interstitial cells on the other hand. He illustrates his views by describing the testicular group and ovarian group of androblastomas as identical tumours and also the testicular group and ovarian group of granulosa cell tumours as identical. But he describes the group of androblastoma tumours in the testis as homologous with the group of granulosa cell group of testicular tumours. He also regards as homologous the same two groups of tumours in the ovary (Table I).

TABLE I

Homologous and Identical Gonadal Tumours after Teilum (1958)



He bases this classification on the fact that testicular tubules and granulosa originate and differentiate from the same mesenchyme. The development not only of androblastomas but also of tumours of the granulosa cell group in either sex may therefore be accounted for in terms of competence of the mesenchymal core of both ovary and testis to elaborate identical neoplasms reflecting the granulosa or the testicular structure.

Burslem, Langley and Woodcock (1954) reported a case in which they could trace histologically definite transition in an ovarian tumour between typical granulosa cells and areas composed of Sertoli cells.

Langley (1957) classifies together the fibroma, thecoma, granulosa cell tumour, Sertoli cell tumour and interstitial cell tumour. He considers that they all arise from coelomic mesenchyme which retains competence to develop into more highly differentiated tissue. Mackinlay (1957) maintains that granulosa cells and theca cells may change their nature entirely and become lipoid cells producing androgen-like substances or differentiate into Sertoli cells and that the only constant producer of oestrogen is the Sertoli cell.

Langley (1954) describes the case of a woman of 62 who had a Sertoli cell tumour 14·0 cm. in diameter which contained only a few extratesticular Leydig cells. The uterus was absent and ribbons of muscle appeared to represent hypoplastic uterine horns.

Joseph Novak (1943) reported the cases of two sisters aged 27 and 26 years, both without uteri, and with hypoplasia of the external genitalia. Both sisters had bilateral ovarian tumours which were removed and both suffered severe symptoms which seem to have been those of oestrogen-withdrawal. The histological reports indicate Sertoli cell tumours. All the 4 tumours were considerably larger than normal ovaries and it seems reasonable to conclude that they were either hyperplastic or neoplastic. Novak designates his first case "ovotestis". From the histological report and the photomicrographs of the left tumour the appearances are those of a Sertoli cell tumour of the ovary and there does not seem to be any definite evidence of any fully differentiated "ovotestis".

Jolles and Gleave (1945) describe a female of 61 years who in 1932 had a "cryptorchid testis" removed from the inguinal canal. In 1942 a retroperitoneal tumour was removed. It appeared to show features of a Sertoli cell tumour but no interstitial cells were seen in it. The patient died of multiple secondaries which

were anaplastic and appeared sarcomatous. The vagina was 2·5 cm. long and appeared smooth. At autopsy there was no trace of a cervix or uterus. The apparently benign tumour originally removed may have been a Sertoli cell tumour but the authors have no detailed histological report.

Goldberg and Maxwell (1947) published a brief report without histological detail of a 19-year-old female of eunuchoid build, large breasts, poorly-developed external genitalia, rudimentary vagina and absence of the uterus and cervix. The urinary gonadotrophins were "high". At laparotomy bilateral rudimentary structures were found suggesting the unfused anlage of a uterus together with bilateral poorly-developed gonads which were removed. They were "a highly differentiated arrhenoblastoma" and macroscopically resembled adrenal cortex. The authors noted the well-developed breasts which they considered were the result of oestrogen stimulation. There would thus seem to be a group of 6 cases in all in which a lesion of the ovaries is linked with congenital absence of the uterus. The gonad of our own case closely resembles Langley's case and Novak's two cases histologically; Goldberg and Maxwell's case and Jolles and Gleave's case may also belong to this group although there is some doubt as to whether in these two cases the tumours were in fact composed of Sertoli cells. Apart from their original case Goldberg and Maxwell found 7 similar cases in the literature (Schneider *et al.*, 1952). Schneider *et al.* have found 6 further cases in the literature and have reported as well 6 cases of their own. Many of these cases have not been confirmed histologically or illustrated by adequate photomicrographs and in fact only two of the cases of Schneider and his colleagues are confirmed and illustrated histologically. A number of reports of the "Goldberg-Maxwell Syndrome" have also been collected by Rama Vaish (1958) who added 3 cases of his own. The descriptions of the histology in these reports are sparse and there are no illustrations. They are, therefore, unacceptable as proven Sertoli cell tumours.

Stalker and Hendry (1952) collected 17 cases of tubular adenoma of the testis and reported that 11 of these cases occurred in pseudohermaphrodites. They considered that some of the Sertoli cell lesions in their collected cases were in fact hyperplasia of the Sertoli cells rather than true adenomata, though they considered their own case to be a true tumour. It seems possible that some of these cases may be related aetiologically to the case described in this paper.

The sections of Mrs. K.J.'s gonad were histologically indistinguishable from a Sertoli cell tumour of the ovary. Her case and other similar cases differ from those of Sertoli cell tumours described by Teilum and others in that Teilum's cases were all in women with properly developed uterus, tubes and vagina. Teilum's cases are accepted as neoplasms whereas those cases similar to Mrs. K.J. have usually been reported as "cryptorchid testes".

Langley (1957) postulated that during the indifferent stage of development of the gonad a disturbance of the hormonal environment causes a genetically female cell to develop in the male direction thereby producing a "testis-like" structure in the place of the ovary. Langley (1954) suggests that such a lesion should be regarded as a Sertoli cell hamartoma. It seems likely on experimental evidence that a similar hormonal influence could also cause aplasia of the uterus (Jost, 1958).

Masson (1956) defines as hamata, lesions consisting of tissues belonging to the region where they are found, but which have eluded the organized development of that region. Furthermore if such a lesion is endowed with sufficient "embryonic vigour", it will develop into a structure whose growth is limited in time and space and so becomes a hamartic tumour or hamartoma.

Mrs. K.J. might be described as a case of "pseudohermaphroditism" though this seems now to be an outmoded classification. Her chromosomal sex is female and she therefore should be regarded as a female with maldevelopment of the gonads (Sertoli cell hamartoma) and uterine aplasia.

Some cases with aplasia of the uterus and "cryptorchid testis" have been described as Turner's Syndrome or gonadal dysgenesis. The majority of the 22 cases whose chromo-

somes were sexed by Grumbach, Van Wyk and Wilkins (1955) were male but 2 were female. Mrs. K.J. does not appear to be an example of this condition as none of the other stigmata of Turner's Syndrome were recognized in her.

Mrs. K.J.'s production of pregnanediol, gonadotrophin and 17-ketosteroids after her laparotomy was within normal limits for a post-menopausal woman but there is no indication as to what it may have been prior to her operation apart from her statement that she has never suffered from hot flushes nor had to shave. The only abnormal finding in fact had been slight but definite scantiness of her axillary and pubic hair. It is unlikely that a second gonad was overlooked at laparotomy. The hormonal output was estimated some time after this event and therefore is in fact the output of a person without gonads. There were no oestrogen withdrawal symptoms after the operation to suggest that oestrogen production may have been significantly higher beforehand. Sertoli cells, it is generally accepted, produce oestrogen. In this case the majority of the cords of Sertoli cells were immature and therefore may have produced little hormone.

The chromosomal sex of Mrs. K.J. was female. This is in accordance with the findings in Sertoli cell tumours (Teilum, 1958) but evidence is lacking on this point in other accepted cases of Sertoli cell hamartomata.

Summary

The case of a woman with congenital absence of the uterus and a Sertoli cell hamartoma of the ovary is reported. Similar cases have been found in the literature. Current theories about the development and classification of these hamartomas are reviewed.

Acknowledgments

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OLEO-KERATIN GRANULOMA IN PERITONEUM: A RARE COMPLICATION OF OVARIAN DERMOID

BY

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INTRODUCTION

CHRONIC giant cell granulomata represent the typical response of the body to a varied range of noxious or irritant agents acting at a low level of toxicity. Among the very long list that could be made of such agents it is somewhat surprising that two substances made by the organism itself, keratin and sebum, are amongst the most potent granuloma producers. Keratin granulomata are well recognized and not uncommon in skin and oral mucosa.

Rarely, but then often disastrously, keratin and sebum gain access to the peritoneum. The source is always a dermoid cyst of the ovary which has suffered some form of damage, either infarction or rupture. Not infrequently this accident occurs during pregnancy (Bell and Wilson, 1955; Van Orman and Mautner, 1951) or during labour. Some 40 cases of intra-peritoneal oleo-keratin granuloma due to damaged dermoid cysts have been reported, the earliest by Barth in 1843. In view of the rarity of the condition, and because of the possible seriousness of the sequelae, the following case is presented.

CASE REPORT

Mrs. O'H., was a primigravida, aged 19, with pre-eclamptic toxaemia. She was admitted as an emergency in labour near term because the foetal head was not engaged in the pelvis. She proceeded slowly in labour from the night of admission, the 13th June, 1958. On the following day, when the cervix had been fully dilated for an hour it was thought appropriate to undertake a forceps delivery under general anaesthesia because of inadequate progress. Vaginal examination preparatory to this operation showed a pelvic tumour which had not been recognized at any of the previous examinations which had been carried out without anaesthesia. This tumour was palpated through the posterior vaginal wall and appeared to be a flaccid mass in the pouch of Douglas. A forceps rotation and delivery was performed past the tumour when it had been displaced from the pelvis, and a living female infant in a satisfactory condition was born. A manual removal of the placenta was carried out, the genital tract explored digitally to exclude injury and the tumour palpated again bi-manually. This examination of the tumour showed that it was not collapsed after delivery and that it was probably a mobile swelling of the ovary. An episiotomy was repaired and the mother transferred in good condition to a lying-in ward. Following this birth, which had caused no surgical shock, the mother was quite well until the fifth puerperal day, when an irregular high pyrexia commenced, at first accompanied by some diarrhoea. There were no symptoms nor physical signs pointing to the cause of the pyrexia and cultures of stool and urine specimens were unrewarding. The pyrexia continued (without further bowel symptoms) and the mother was treated presumptively with tetracycline. In the early days of her pyrexia she had a polymorphonuclear leucocytosis but the total white cell count shortly fell from 32,000 to 10,000 per c.mm. An X-ray of the chest showed no abnormality and a high vaginal swab provided no useful information. Although there were no physical signs present in the abdomen, the absence of any other cause for her pyrexia led it to be assumed that some accident had affected the pelvic tumour, and a laparotomy was carried out on the 27th June, the thirteenth day of the puerperium. There had been no pre-operative clinical signs to indicate peritonitis and it was surprising to find free fluid in the abdomen at operation and extensive fresh fibrinous adhesions. The pelvic tumour was found and removed with considerable difficulty because of a

FIG. 1

The cyst, partly opened, showing dermoid contents and exudate on the surface.

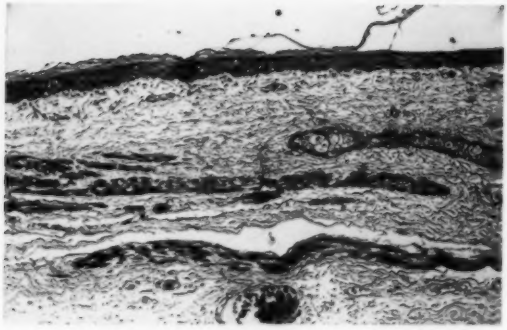

FIG. 2

An unaffected part of the cyst wall showing the usual pattern of a dermoid. ×50.

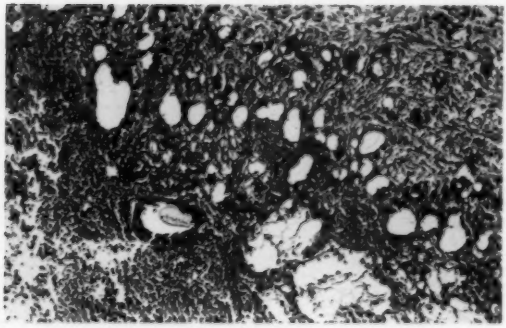

FIG. 3

Foreign body giant cell granuloma showing a hair shaft and loose keratin. ×50.

severe inflammatory peritoneal reaction. The parietal peritoneum and visceral serous coats, as far as they were exposed, were oedematous, covered by fibrinous exudates and mutually adherent. The abdomen was closed without drainage and the pelvic tumour, which had proved to be a dermoid cyst of the left ovary, was submitted for pathological examination.

The examination showed that the specimen (Fig. 1) received was a moderately thick-walled cyst, not collapsed, weighing 340 grammes and measuring $11 \cdot 5 \times 10 \times 6 \cdot 5$ cm. It was rather dark red in colour but much of this was obscured by a patchy white exudate which was difficult to scrape off. Cut surfaces showed typical dermoid cyst contents but the sebaceous material was more liquid than usual. No obvious rupture was found on naked eye examination.

Microscopy showed a typical benign dermoid (Fig. 2). The constituents ranged from brain tissue to bone. In many parts of the cyst wall a granuloma composed of some chronic inflammatory cells and many large foreign body giant cells involved all or some portions of the dermoid cyst integument (Fig. 3). Many of the giant cells were vacuolated or contained recognizable fragments of keratin. In addition, where the granuloma involved the serous coat, it was overlaid by a thin fibrino-purulent exudate. Little or no evidence of infarction was present in the cyst.

From the examination of multiple blocks the impression was that some damage to part of the cyst had enabled the contents to spread into the cyst wall unprotected by squamous epithelium, and eventually to the peritoneal surface. The resultant tissue reaction, was, as one would expect, a typical oleo-keratin granuloma.

The condition of the patient after operation was satisfactory for two weeks, although the pyrexia continued at a lower level. After this fortnight the rises of temperature increased in height and an abscess in the laparotomy wound declared itself. This abscess was explored, opened, evacuated and drained on the 18th July. Pus which had been released showed on microscopical examination degenerative pus cells, no *Mycobacterium tuberculosis* nor other organisms; culture yielded neither aerobic nor anaerobic growth. Cultures for *Mycob. tuberculosis* remained sterile. Biopsy of the abscess wall showed fatty tissue with chronic inflammation and only very slight evidence of keratin or other foreign body granuloma. The patient showed an immediate marked improvement following drainage of the abscess. She remained completely apyrexial thereafter and ten days later she was fit to discharge home. She was examined several times as an out-patient, the last occasion being the 22nd January, 1960, eighteen months after delivery. At these visits to the clinic she was well and the pelvis, on vaginal examination, appeared to be normal.

Comment

The interesting feature of the case reported is that pyrexia was the only indication of leakage from the dermoid cyst. There had been no preoperative features which would have led to a diagnosis of peritonitis; indeed the characteristic features of an acute peritonitis were conspicuous by their absence. The usual signs of intra-peritoneal catastrophe, such as rigid tender abdomen, rebound tenderness and toxaemia, were absent. It was only because an ovarian tumour was known to be present that it was decided to open the abdomen in the belief that the tumour must be connected with the otherwise unexplained pyrexia. The findings at laparotomy were attributed to leakage from the dermoid cyst even though this tumour was not collapsed and no point of rupture could be detected. This finding is in keeping with many other reports in the literature. The attribution of the peritonitis to leakage from the dermoid cyst was suggested by histological studies and was confirmed by the subsequent clinical course of the patient. It is reasonable to assume that some trauma occasioned by the operative delivery was responsible for the leakage from the cyst. This assumption necessarily leads to a consideration of the pros and cons of the best method of delivery for this patient. It can readily be argued that she would have been better treated by Caesarean section with removal of the dermoid cyst at that time, than by the method of management that was adopted. The alternative method of treatment, which appears to us to have much to commend it, would have been a laparotomy for removal of the tumour at an earlier stage in the puerperium. It seems in retrospect that this laparotomy, which had been planned, was not undertaken with sufficient urgency. If the laparotomy had been performed during the first five puerperal days, it seems likely that a much less formidable peritonitis would have been encountered. This type of management avoids inflicting on the patient a uterine scar and thereby possibly prejudicing her obstetric future. All things being equal, this latter is the course of management we would advise if a similar case came to our notice again.

Discussion

The rarity of this condition is underlined by the fact that Dr. Magnus Haines of the Chelsea Hospital for Women, Dr. Claude Taylor of

Birmingham and Professor W. St. C. Symmers of Charing Cross Hospital have stated in personal communications that they have no experience of this condition. The subject has been reviewed by Quer, Dockerty and Mayo (1951), who collected 29 cases and added a 30th, of intra-peritoneal rupture of a dermoid cyst. We have found references to 8 further cases in American periodicals since this review. These eight cases include a further review by Kistner (1952) but this almost completely overlaps the above review. The only recent British reference which we have found is a passing mention of the subject by Malpas (1950). The sparsity of these references indicates that it may not be out of place to discuss some of the features of the condition. It has been suggested in the literature that the rarity of rupture of dermoid cysts is explained by their thick wall, but in certain reported cases local areas of thinning in the wall have been observed. In others malignant degeneration has been cited as a possible cause of leakage (Kistner, 1952), but very often no cause could be discovered. In several cases rupture was ascribed to trauma, either from surgery (Evrard and Schneeberger, 1954), including obstetric operations (breech extractions, Quer, Dockerty and Mayo, 1951; Webb, 1955), or from a fall (Piper, 1941). In one case where rupture occurred during pregnancy it appeared to be due to torsion of the cyst (Kistner, 1952). Apart from rupture into the peritoneal cavity infected adherent dermoids may rupture into hollow organs such as the ileum, sigmoid, rectum, bladder or vagina, but only intra-peritoneal rupture is considered here. If rupture of a cyst is acute and its contents become emptied into the peritoneal cavity, shock and generalized peritonitis with possible death may follow.

If the rupture takes the form of a slow leak, or recovery from a more acute episode occurs, then the clinical appearance is somewhat different. The picture which may occur is variable and some of the ways in which these cases have presented according to the reports are as follows:

In a number of cases the accident was evidenced by a stormy puerperium with fever unresponsive to antibiotics and perhaps paralytic ileus with tympanitic abdominal distension (Sax, 1955). In others, there were abdominal symptoms of varying duration including abdominal pain, tenderness and distension (in one case a swollen doughy abdomen for many years), rectal pain, diarrhoea, nausea and vomiting. Other symptoms mentioned are fatigue, 30 pounds weight loss, non-tender abdominal mass, frequency of micturition and jaundice with chills.

At operation the appearances of a diffuse fibro-plastic peritonitis may be confused with either tuberculosis or with carcinoma. In Quer, Dockerty and Mayo's case the patient was at first thought to have inoperable abdominal carcinomatosis. Confusion with tuberculosis occasioned a pelvic clearance by Stein and Kaye (1954) and bilateral salpingectomy by Odle and Rosenburg (1948). One or two American authors have suggested that frozen sections taken at the time of operation may help to overcome this difficulty in diagnosis. In this country, however, the majority of surgeons and pathologists would prefer an adequate biopsy processed by the standard paraffin technique.

At operation the abdomen may be seen to contain oil, serous fluid or cheesy fluid simulating pus. Disseminated cyst contents may be present in this fluid and the presence of hair makes the diagnosis easy. The fluid may be pocketed to form peritoneal abscesses and dense omental and intestinal adhesions may be found. In more long-standing cases, cystic abdominal masses with calcified walls containing sebaceous material may be present and could be mistaken for metastases of a malignant tumour. Alternatively, round yellowish-white peritoneal and omental nodules sometimes occur and simulate tuberculous granulomata. The pre-operative diagnosis is not easy although it might be suspected from the history. Ancillary methods of diagnosis may be of assistance. Paracentesis abdominis might yield characteristic fluid or X-rays may show the shadows of encysted fluid, calcified nodules, teeth or "halos" due to the translucency of fat. Nevertheless, in many cases in the literature there has been a long delay between the presumed time of rupture of the cyst and the establishment of the diagnosis.

Treatment consists of excision of the cyst,

toilet of the peritoneal cavity and aspiration of free fluid. Sometimes drainage of a large abscess, or multiple abscesses, must be undertaken. The nature of the intra-peritoneal adhesions that are encountered is such that they have to be left alone. Treatment is sometimes long delayed and various sequelae are recorded. In cases of long standing it is possible that ascites requiring frequent paracentesis may arise, that intestinal obstruction may occur or that secondary pyogenic infection may supervene. Malignant degeneration has also already been referred to as a possible sequela. In certain of the cases reported, these sequelae have led to prolonged invalidism, major disablement and even to death from peritonitis.

Conclusion

The serious nature of the possible sequelae leads us to emphasize the following points:

(1) Dermoid cysts should never be tapped at operation. They should be removed with great care to avoid soiling the peritoneum with their sebaceous contents.

(2) It is important to inspect the ovaries at the time of Caesarean section. This was a precaution omitted by the authors of one of the case reports which we have read.

(3) Ovarian cysts should be sought for in early pregnancy and whenever diagnosed, removed promptly.

Summary

The occurrence of an oleo-keratin granuloma due to a dermoid cyst is reported. In the case described there was a severe but apparently benign peritonitis. The case is used to introduce discussion and a review of a rare but potentially serious complication of an "innocent" ovarian tumour.

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CORONARY OCCLUSION IN LABOUR

BY

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CORONARY occlusion occurring during labour is one of the rarest of obstetrical complications. Mendelson (1952) in a review of the literature recorded only one case. Since that case, reported by Katz (1922), no further reports have been discovered in a review of the literature to date. For this reason the following case is considered worthy of record.

CASE REPORT

The patient was age 29 years, para-1, gravida-3. She had one normal pregnancy three years previously terminating in a forceps delivery of a male child weighing 6 pounds 8 ounces. This child had an imperforate anus treated by operation but was otherwise normal and was alive and well at the time of her third pregnancy. Two years previously she aborted a 22-weeks pregnancy.

Her previous history was negative apart from a dilatation and curettage following her abortion. She had no previous medical illness or operations.

Her family history revealed nothing significant. There was no history of hypertension or diabetes.

She first attended the antenatal clinic on 24th July, 1959, being then about 34-weeks pregnant. Her estimated date of delivery was 2nd September, 1959. She had previously been attending another hospital and at her first attendance there, on 10th March, her blood pressure was recorded as 130/90, her urine had contained no albumin, she had no oedema and her blood group was AB, Rhesus positive. A chest X-ray had revealed no cardiac or respiratory abnormalities. Her medical practitioner reported that in early June she had gained an excessive amount of weight and her blood pressure had risen to 140/90, but without albuminuria. He treated her by confining her to bed, restricting her fluid and salt intake and by administering chlorothiazide.

On 24th July, her blood pressure was 130/90, the urine was clear and there was some oedema. The haemoglobin was 94 per cent. The weight was 11 stones 3 pounds. The foetus was lying transversely and was turned to a vertex position. Physical examination revealed no abnormalities of the respiratory or cardiovascular systems.

She attended the antenatal clinic regularly and, apart from a rise of blood pressure to 140/85 accompanied by slight ankle oedema at the 38th week which responded to rest, she remained normal. On 2nd September her blood pressure was 125/85, the urine was clear and the weight was 11 stones 8 pounds. She had no ankle oedema. The foetus was presenting as a vertex with the head free above the pelvic brim in the right occipito-anterior position.

She was admitted to hospital on 4th September having weak irregular contractions. These however ceased shortly after admission. Her blood pressure was 130/90.

On 6th September there was no sign of labour starting and a medical induction, consisting of castor-oil, a hot bath and an enema, was administered. This was unsuccessful.

On 8th September, in view of her postmaturity and slight hypertension (blood pressure 135/90) labour was induced by surgical rupture

of the membranes using a Drew Smythe catheter.

On the morning of 9th September the ward sister reported a slight irregularity of the patient's pulse but further examination did not confirm this and a complete physical examination revealed no cardiac or respiratory abnormality.

Uterine contractions commenced at 4.30 p.m. on 9th September and rapidly became strong and regular at two-minute intervals. At 5 p.m. rectal examination revealed that the cervix was a quarter dilated. At 5.45 p.m. the cervix was half dilated with the head in the mid-cavity of the pelvis. The maternal pulse rate was 92 and the foetal heart rate 140 per minute.

At 6 p.m. the patient started passing large quantities of heavily meconium-stained liquor *per vaginam* and the foetal heart rate dropped rapidly to 80 per minute. Following immediately upon this the patient became breathless and cyanosed and her pulse rate became irregular and weak at 90 to 100 per minute.

The patient's condition rapidly deteriorated, the uterine contractions ceased and the patient complained only of slight continuous epigastric pain. Her cyanosis and dyspnoea increased. Physical examination revealed no signs of any abdominal or uterine abnormality. The foetal heart was not heard. The maternal heart sounds were faint but otherwise normal. The blood pressure was 100/60, the temperature 99·8° Fahrenheit. There were numerous moist sounds in the bases of both lungs. Central cyanosis was marked. A diagnosis of cardiac failure with acute pulmonary oedema was made.

The patient was placed in a sitting position and oxygen administered. She was given morphine, grains $\frac{1}{4}$ intramuscularly and Digoxin, 0·5 milligram intravenously. Despite treatment the patient soon became unconscious and died undelivered at 6.45 p.m.

A post-mortem examination was performed the following day and disclosed a thrombosis of the left coronary artery with complete occlusion $1\frac{1}{2}$ inches from its aortic origin. The death certificate as issued by the coroner gave the cause of death as left-sided cardiac failure and pulmonary oedema due to coronary thrombosis.

Discussion

Considering that the cardiac output rises during the first stage of labour, is increased by pain and anxiety and may even rise as much as 30·9 per cent during effective uterine contractions (Hendricks and Quilligan, 1956), it is not surprising that coronary thrombosis occurring at this time should be disastrous and rapidly fatal.

The diagnosis may be difficult, the characteristic pain may be absent or, as in the case reported, may be only slight and overshadowed by the pain of uterine contractions. Other symptoms, such as shortness of breath, lowering of the pulse pressure, pyrexia, drop in blood pressure and faint heart sounds, may easily be overlooked in the course of a progressive labour. The onset of cardiac failure and pulmonary oedema will suggest the diagnosis probably too late for effective treatment.

Summary

A case of coronary thrombosis occurring during labour is described.

The rarity of this condition is noted and comment is made on the difficulty in making a diagnosis and of initiating effective treatment.

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RADIAL PALSY SIMULATING VOLKMANN'S CONTRACTURE IN A NEWLY-BORN BABY

BY

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AND

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ATTENTION has been previously drawn to the occurrence of neuropraxia in the form of radial nerve palsy in the newly born (Craig and Clark, 1958). This contribution describes an example of radial nerve palsy which differed from those previously recorded in temporarily simulating a classic Volkmann's ischaemic contracture.

CLINICAL FINDINGS

Baby H., female, birth weight 6 pounds 2 ounces, had an estimated gestation period of 39 weeks. Presentation, vertex. Labour induced on account of pre-eclampsia by artificial rupture of membranes. Pitocin was administered later on account of slow progress. Episiotomy was performed. The delivery was spontaneous. The mother was 30 years old and this was her first pregnancy.

At birth the baby's general condition was satisfactory and regular rhythmic respirations were established at once. When examined ten minutes after delivery the infant was noted to have a right wrist drop (Fig. 1). Discoloration and bruising were features of the lateral supracondylar aspect of the right upper arm, and the right lateral aspect of the thorax (Fig. 2). The affected tissues in the arm and thorax were in approximately the same horizontal plane. Those in the arm were characterized by purple discoloration, slight depression of the skin surface with apparent adhesion of the skin to deeper structures which were slightly indurated. In some respects the local findings in the arm resembled those of scleroderma. By way of contrast the lesions in the wall of the right thorax consisted of uncomplicated contusions.

Re-examined at the age of 36 hours signs were observed suggestive of shortening of the flexor tendons of the right hand. Extension of the wrist was accompanied by flexion of the fingers, and flexion of the wrist was accompanied by extension of the fingers (Fig. 3). Movements at the elbow and shoulder joints were normal. The radial pulse was readily palpable. No local treatment was instituted but the infant was kept under periodic observation. At the age of 5 weeks the findings were unchanged except in that there were extremely limited voluntary movements of the wrist and fingers of the right hand. Signs suggestive of shortening of the flexor tendons disappeared by the age of 8 weeks and those of wrist drop by the age of 3 months. The sclerematous area on the right arm disappeared gradually and was no longer visible within 2 months of birth. Recovery was confirmed as being complete at the time of final examination at the age of 4 months.

FIG. 1
To show drop wrist and abrasion on chest wall.

FIG. 2

To show the abrasion on the outer aspect of the elbow. This mark corresponds with the level of the similar lesion on the chest wall.

FIG. 3

To show the drop wrist and apparent flexion contracture of the flexor muscles of the forearm.

Discussion

In this infant a provisional diagnosis of Volkmann's contracture was made on the single clinical finding of apparent shortening of the flexor muscles of the right wrist and fingers. A number of considerations however pointed to the inaccuracy of the diagnosis. Thus the radial pulse was readily and constantly palpable and there was no demonstrable oedema of the affected arm and hand.

Although there was conclusive evidence of antenatal compression of the right upper arm and thorax in the visible contusions at birth, the contusions of themselves did not warrant the assumption that there had been peripheral ischaemia of sufficient severity to substantiate a diagnosis of Volkmann's contracture. In point of fact the evidence of superficial bruising closely resembled that already reported in newly-born babies with peripheral radial nerve palsies (Craig and Clark, 1958). Furthermore, the spontaneous, complete functional recovery of the apparently contracted muscles is not compatible with the provisional diagnosis of ischaemic contracture. Fibrous tissue formation and progressive inextensible contracture take place in the affected fibres of infarcted muscle. It is difficult to accept that vascular deprivation of muscle could be unaccompanied by infarction if shortening of the affected muscles is attributable to the vascular lesion. Nor is it reasonable to account for apparent shortening of the flexor muscles in a forearm by impaired peripheral circulation in the constant presence of a palpable radial pulse.

We have been unable to discover any convincing recorded evidence of the occurrence in newly-born babies of Volkmann's contracture in association with nerve lesions. In an article entitled "Neonatal Volkmann's Contracture" Bedbrook (1953) describes a surviving twin, newly delivered by Caesarean section, with marked flexure contraction of the right wrist and fingers and flaccid paralysis of the whole right upper limb. The affected limb was oedematous but the radial pulse was present. Functional recovery was complete by the age of 4 months. Bedbrook was of the opinion that the infant had an ischaemic contracture together with a concomitant brachial plexus lesion. Adequate evidence of ischaemic contracture is lacking. As in the baby described by us in this article, the complete functional recovery, the constant presence of a radial pulse and the localization of the palsy to the distribution of the radial nerve are all arguments strongly favouring inclusion of the lesion in the group of neonatal peripheral neurapraxias described in this journal in 1958.

Summary

The occurrence in a newly-born baby of radial nerve palsy temporarily simulating Volkmann's ischaemic contracture is described.

Acknowledgments

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CARCINOMA OF THE BODY OF THE UTERUS AT CHELSEA HOSPITAL FOR WOMEN, 1943–1953

BY

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RECENTLY there has been much discussion about the choice of treatment for carcinoma of the body of the uterus. With the object of trying to assess the results obtained by different methods of treatment all the cases of this disease which were seen at Chelsea Hospital for Women and at the Royal Marsden Hospital during the years 1943–1953 have been reviewed. The two hospitals have a combined clinic for gynaecological cancer, to which some of the cases were referred from other hospitals, but the majority of cases came from the ordinary out-patient department of the Chelsea Hospital for Women.

TABLE I

Ages	Number of Cases
30–39	4
40–45	17
46–50	31
51–55	43
56–60	44
61–65	41
66–70	20
71–75	8
76–80	9
81–85	2

CLINICAL MATERIAL

A total of 223 cases were studied, and all of these have been followed for at least five years after treatment. The ages of the patients are shown in Table I, and the distribution is as would be expected.

TABLE II

	Cases
Menopause not reached	45 (27%)
Menopause between ages:	
30–39	5
40–45	17
46–50	41
51–55	51 (73%)
56–60	8
70	1
Uncertain or unstated	55

The ages at which the patients reach the menopause are shown in Table II. It will be seen that in 27 per cent of the cases the disease was discovered before the menopause had been reached.

In this series the ratio of cases of carcinoma of the cervix to carcinoma of the body of the uterus varied between 3·7 : 1 and 2·2 : 1.

Among these patients 60 per cent had been pregnant.

ASSOCIATED CONDITIONS

In this series diabetes was found in 3 patients (1·3 per cent). Blood sugar curves were not routinely performed. This is a lower incidence than that reported by Vander (1958) who found an incidence of 5 per cent, and by Way (1954) who found diabetes or abnormal glucose tolerance curves in 29 per cent of his cases.

It has been suggested that the use of intra-uterine radium to induce an artificial menopause

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TABLE III

Total number of cases seen: 223. Five-year survival: 143 (60·4%)

Stage	Number of Patients	Percentage of Total
I	147	65·9
II	28	12·5
III	24	10·7
IV	24	10·7

Stage I

Type of Treatment	Number Treated	Five-Year Survival
Total number: 147 Five-year survival: 114 (77·5%)		
TH and BSO* alone	103	82 (80%)
TH and BSO with vaginal radium	16	12 (80%)
TH and BSO with high voltage therapy	15	13 (86%)
Radiotherapy alone	10	5 (50%)
Wertheim hysterectomy	1	
Subtotal hysterectomy	1	
Diagnostic curettage followed by death	1	

Stage II

Total number: 28 Five-year survival: 19 (68%)		
TH and BSO alone	7	5
TH and BSO with vaginal radium	4	3
TH and BSO with high voltage therapy	4	4
Radiotherapy alone	5	3
Wertheim hysterectomy	3	1
Wertheim hysterectomy with high voltage therapy	3	2
Extended total hysterectomy	2	1

Stage III

Total number: 24 Five-year survival: 10 (42%)		
TH and BSO alone	11	4
TH and BSO with high voltage therapy	9	5
TH and BSO with vaginal radium	2	0
Wertheim hysterectomy	1	1
Extended total hysterectomy	1	0

Stage IV

Total number: 24 Five-year survival: 0		
Palliative radiotherapy	12	
TH and BSO alone	6	
Laparotomy only	7	(subsequent radiotherapy given to 3 cases)
No treatment possible	2	

There were 7 deaths from intercurrent disease, all in cases with Stage I growths.

* TH and BSO=Total hysterectomy and bilateral salpingo-oöphorectomy.

may increase the risk of development of carcinoma of the body of the uterus. Taylor and Becker (1947) found that 5 per cent of cases of carcinoma of the body had had a previous radium menopause, while Palmer and Spratt (1956) in a large statistical analysis found that carcinoma of the body of the uterus occurred 6 times more often after a radium menopause than in a group of women who had a natural menopause. Turnbull (1956) reported a series of cases from Aberdeen in which a radium menopause had been induced, and in 124 cases of carcinoma of the body he found that 4 per cent had previously been treated by the induction of a radium menopause. He found no evidence that radiation increased the risk of cancer developing in the pelvis, but since the uterus is not removed the chance of malignant change in a patient who is predisposed to it still exists. In the present series only 3 patients (1·3 per cent) had had a previous radium menopause.

Granulosa cell tumours were present in 5 cases in the present series, and 2 of these also had associated theca cell tumours. Dockerty and colleagues (1951) reported the association of these tumours with carcinoma of the endometrium, but a large series of granulosa cell tumours is necessary before a true cause and effect relationship can be proved or disproved.

Jackson and Dockerty (1957) describe carcinoma of the endometrium in association with the Stein-Leventhal syndrome, and this association was noted in 1 case in this series.

Staging

To compare different treatments it is necessary to compare comparable cases, but unfortunately no completely successful method of staging has yet been devised for carcinoma of the body of the uterus.

The present international classification divides the cases into two stages; Stage I in which the growth is confined to the uterus, and Stage II when growth has spread outside the uterus and is inoperable. Stage I is further divided into two subgroups; Group I in which the case is clinically operable, and Group II in which the case is inoperable because of the age or ill-health of the patient. This subgrouping is not very satisfactory because surgeons hold such differing opinions about operative risk.

It is not possible to predict accurately the extent of the disease by clinical examination, for it is often only on microscopical examination that one can detect secondary deposits in the ovaries or extension of the growth into the cervix. Rickford (1954) and Blaikley, Kottmeier, Martius and Meigs (1958) have suggested different methods of clinical staging, but all the authors acknowledge the difficulties mentioned above.

It is useful to have a pathological classification which can be used to present the results of varied treatment for comparable stages of the disease, and the following classification has been used in all the cases in this series:

Stage I. Carcinoma confined to the corpus (endometrium and/or myometrium).

Stage II. Carcinoma corporis, also involving the cervical canal.

Stage III. Carcinoma confined to the pelvis (spread to ovaries, tubes, and/or broad ligaments).

Stage IV. Involvement of other organs (vagina, bladder, large gut or distant metastases).

Except in 29 cases which did not have a laparotomy, and in which staging was therefore based on clinical observation, this classification was based on the actual extent of the disease, nearly always established by microscopical examination of the extirpated uterus, tubes and ovaries. The number of cases in the different stages are shown in Table III. This shows the various methods and combinations of treatment employed, together with the five-year survival rates. Radiotherapy was seldom used alone, but usually as an adjunct to surgical treatment.

Histology

Table IV shows the type of growth found in these cases. The vast majority (89 per cent) were adenocarcinomata of moderate or well-defined differentiation. It will also be seen that the histological finding of an anaplastic growth does not necessarily mean a poor prognosis. If such

TABLE IV

Summary of Histology (221 Cases)

	Cases
Adenocarcinoma, well differentiated	197 (89%)
Anaplastic growth, or poorly differentiated adenocarcinoma	21 (10%)
Squamous celled carcinoma	3 (1%)
Of the anaplastic carcinomata:	
In Stage I there were 12 cases, and 11 of these survived 5 years	
In Stage II there were 4 cases, and 4 of these survived 5 years	
In Stage III there was 1 case, and 0 of these survived 5 years	
In Stage IV there were 4 cases, and 0 of these survived 5 years	

a growth is in an early stage the outlook is not adverse, and too much weight should not be given to a report of an anaplastic growth.

COMPARISON OF RADIOTHERAPY AND SURGICAL TREATMENT

It is generally held that surgical treatment alone gives better results in this disease than radiotherapy alone. The results for Stage I cases support this (Table III), but the figures are too small to prove it. To add to the number of cases available for study the records of the Royal Marsden Hospital for the years 1943–1953 were studied, and 172 additional cases were thus obtained. The majority of these cases were referred from "outside" hospitals for (*a*) prophylactic post-operative radiotherapy, (*b*) treatment of recurrent growth, or (*c*) for palliative radiation when the primary growth was inoperable. There were only 17 cases in which primary curative treatment was attempted by radiotherapy alone. Clinical staging showed growth apparently confined to the uterus in all these cases. The indications for using radium rather than surgery were combinations of advanced age, obesity and hypertension. These contra-indications to surgical treatment are of course relative, and in 4 of these cases growth recurred and the patients eventually submitted to, and survived, surgical treatment although the original "contra-indications" were unchanged. Of these 17 patients 8 survived for 5 years or more. There were 2 deaths from intercurrent disease.

If these 17 cases from the Royal Marsden Hospital are added to the 15 cases from Stages I and II (Table III) from the Chelsea Hospital for Women treated by radiotherapy it will be seen that out of a total of 32 cases 16 survived for 5 years, but as already stated 4 of the cases required surgical treatment for recurrence of growth in the uterus. It would appear that whenever possible surgical treatment is to be chosen.

The best results in this series occurred from combination of primary surgical treatment with radiotherapy. Two problems of surgical treatment need special consideration, namely, recurrence in the vaginal vault and involvement of lymphatic glands.

Vaginal recurrences (Table V). Recurrences of growth in the vaginal vault after operation for carcinoma of the body of the uterus are an important problem, and their origin is uncertain. They may be due to a spill and implantation of cancer cells at the time of operation, or to growth of cells which have been left behind in either the vaginal wall itself or in the adjacent lymphatics. Venous spread, similar to that of chorionepithelioma from the uterus to the vagina, is also a possibility.

Among the cases in Stage I there were 8 vaginal recurrences, an incidence of 1 in 13; but when the operation was combined with radiotherapy the incidence fell to 1 in 31. Kottmeier (1955), using post-operative vaginal radium in Stage I growths, has also shown the efficacy of this treatment by reducing his vaginal recurrences to 2·3 per cent.

TABLE V

Local Recurrences After Treatment

Stage	Treatment	Number Treated	No. with Recurrence	Site of Recurrence		
				Vault	Pelvic Wall	Sub-urethral
I	TH and BSO* alone	103	8	8		
	TH and BSO and high voltage therapy	15	1	1		
	TH and BSO and vaginal radium	16				
	Wertheim hysterectomy	1				
	Subtotal hysterectomy	1				
	Radium and vaginal hysterectomy 3 years later	1	1	1		
	Radiotherapy alone	9				
II	TH and BSO alone	7	2	1	1	
	TH and BSO and high voltage therapy	4				
	TH and BSO and vaginal radium	4				
	Wertheim or extended hysterectomy	5	3		3	
	Wertheim hysterectomy and high voltage therapy	3				
	Radiotherapy alone	5				
III	TH and BSO alone	11	2	2		
	TH and BSO and high voltage therapy	9	1			1
	TH and BSO and vaginal radium	2	1		Vulval	
	Wertheim or extended hysterectomy	2				

* TH and BSO=Total hysterectomy and bilateral salpingo-oöphorectomy.

In Stage II cases, in which the cervix was involved, it is notable that the recurrences tended to appear on the side wall of the pelvis rather than in the vaginal vault; that is, the growth behaves in the same way as carcinoma of the cervix.

In Stage III there was a higher incidence of recurrences, but the spread was of the same pattern as in Stage I. Suburethral recurrence occurred in one case in Stage III, and in other Stage IV cases.

The cases were hardly numerous enough to prove the value of the vaginal application of radium in preventing recurrence of growth in the vaginal vault after hysterectomy, but if Stages I to III are taken together the evidence is at least suggestive. After 121 ordinary total hysterectomies (without radium) there were 12 cases of recurrence in the vaginal vault, and in 11 of these the recurrence appeared within a year. After 31 total hysterectomies, which were preceded or followed by the vaginal application of radium, no vault recurrence was seen.

Involvement of lymphatic glands. Hitherto it has not often been the practice to excise lymphatic glands during operations for carcinoma of the body of the uterus, so that the degree of involvement of the glands has been unknown. Between 1943 and 1958 Wertheim's hysterectomy has been performed in Chelsea Hospital for Women 27 times for this disease. In addition glands have been removed or biopsied in another 6 cases, and they were also examined in a patient who died of pulmonary embolism after diagnostic curettage. Thus the glands were examined histologically in 34 cases, and in 10 of these (29 per cent) were involved by growth. In Stage I, 5 out of 22 cases were involved; in Stage II, 2 out of 8; and in Stage III, 3 out of 4. Winterton (1959) reported on 99 Wertheim operations for carcinoma of the body of the uterus, and found that the glands were involved in 9 per cent of his cases. Gusberg (1959) compiled figures for node involvement which had been published by five authors, and the incidence varied from 17 to 33 per cent in groups of cases whose numbers

varied from 20 to 64. All these figures support the statement of Willis (1952) that previous estimates of lymphatic node involvement in this disease have been erroneously low.

Surgical Treatment

The results obtained have already been set out in Table III. If Stage IV is excluded, because in that stage only palliative treatment is possible, then 199 cases remain, of which 119 (60 per cent) survived 5 years. Unfortunately there is no reliable clinical means of determining whether an operable case is in Stage I, II or III. At the Cancer Congress in London both Hawksworth (1959) and Gusberg (1959) were concerned with this difficulty of staging.

Fractional curettage was at first thought to be of some use in differentiating between Stages I and II, but in practice this has not proved to be so. Sometimes growth oozes out of the cervix when a dilator is inserted and it is impossible to be sure where it is coming from while on other occasions growth thought to be originating from the cervical canal is afterwards shown to be from a polypoid downward projection from the body of the uterus.

We have already seen that the lymph nodes are involved by growth in perhaps 20 per cent of cases, and the logical way to deal with these nodes is by Wertheim's hysterectomy, as it seems very doubtful whether radiotherapy can kill all the cancer cells in such nodes. Wertheim's hysterectomy carries an increased operative mortality and a risk of urinary fistulae, and these risks must be weighed against the hope of saving some of the patients who have involved nodes. Corscaden and Tovell (1954) say that there is no improvement in the salvage rates, while Schwartz and Brunschwig (1957) report that only 2 patients out of 13 with positive nodes treated by Wertheim's hysterectomy survived 5 years. However, these figures are not truly comparable with the present series, since the staging is not by the same method, and the degree of spread of the growth is not stated.

In this hospital between 1943 and 1958 Wertheim's hysterectomy was performed 27 times for carcinoma of the body of the uterus. There were 2 operative deaths, but no fistulae. Winterton (1959) reported that in 99 operations there were 3 operative deaths and one fistula. His series showed a 5-year survival rate of 76 per cent. Winterton's figures are most impressive, and when corrected to exclude those patients who died of intercurrent disease the cure rate is 84 per cent. This is a good indication of what can be achieved by this operation, but owing to the difficulty of staging it is not possible to compare these figures directly with any other series. Until a series of cases has been accurately staged and followed up after being treated by Wertheim's hysterectomy it will not be possible to decide whether the added risks of the more extensive operation are justified by an increased salvage rate for those patients with involved nodes.

Wertheim's hysterectomy might be chosen for Stage II cases, for there is evidence to suggest that, if the cervix is involved by growth, then the parametrium is also likely to be involved, and only Wertheim's operation will adequately clear it. The difficulty is that there is often no certain evidence of the cervical invasion, and we have already stated that fractional curettage is unreliable.

The operation of "extended total hysterectomy" has been suggested as a treatment for carcinoma of the body of the uterus. By this term most surgeons only mean that they take away a little more of the vagina in an effort to prevent vault recurrence, but this is much better done by the application of radium. If the operation is to be extended it is surely logical to perform Wertheim's operation, in which the lymph nodes are removed, and also more parametrium and vagina.

It would appear from the results already given that, although radiotherapy has not been given a very extensive trial, it does not appear to be adequate treatment. A combination of surgery and radiotherapy gives better results than either employed alone, and this is particularly noticeable when the question of vaginal recurrence is considered, a conclusion that Bourne and co-workers (1955) reached in their report on a series of cases from Montreal.

The scheme of treatment at present in use in the combined Cancer Clinic of the two hospitals is two Stockholm applications of radium at a

fortnight's interval, followed two weeks later by operation. At each application an intrauterine tube containing 50 mg. of radium, and two vaginal packets containing 20 to 35 mg. each, depending on the particular case are used, and left in place for 22 hours. It is believed that pre-operative radium is preferable to post-operative application because (*a*) it is easier to apply, (*b*) it gives a better dose distribution, which is important if the growth is involving the cervix, and (*c*) it minimizes the risk of spill at operation. It has not been found that pre-operative radium makes the operation more difficult. From the preceding results the operation of choice would appear to be total hysterectomy and bilateral salpingo-oöphorectomy, but if the operative scope is to be widened then there are reasonable grounds for performing Wertheim's hysterectomy. This is especially suggested if there are grounds for suspecting that the cervix is involved.

Summary

The results are given of a 5-year follow-up of 223 cases of carcinoma of the body of the uterus.

A classification based on histological findings is used and results for the various stages of the disease are given. It is shown that the addition of radiotherapy to surgery improves these results. Figures for involvement of lymphatic glands and of local recurrence are given, and the choice of operation is discussed.

I would like to thank all the surgeons of the Chelsea Hospital for Women and the Staff of the Royal Marsden Hospital for permission to report their results. I am grateful to Mr. R. B. K. Rickford and Mr. S. G. Clayton for much assistance, and to Mr. J. B. Blaikley for generous advice and encouragement.

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VACUUM-EXTRACTION

With a Report of 10 Cases

BY

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IN 1953 and 1954 Malmström in Sweden published the first results he had obtained with the vacuum-extractor (v.e.) or suction cup, a new obstetrical instrument which he had designed. It was later developed further and got its final form as described in Malmström's thesis in 1957.

It is assumed that contractions of the uterus can be caused or intensified by the pressure upon the cervix created by the presenting part of the foetus. For this reason the scalp traction clamp has been used since 1931 in cases of uterine inertia (Kühnel, 1940; Evelbauer, 1956, 1958). The results have not been encouraging, and Douglass *et al.* (1953), who studied the use of the Willet clamp in cases of uterine inertia by means of a tokodynamometer, found no change in intensity, frequency, or duration of uterine contractions. The traction is to be limited to a power of 1 to 1·5 kg. in order to avoid the risk of the scalp being torn off. The original intention of the v.e. was to intensify uterine contractions by means of traction upon the presenting head in cases of uterine inertia. Later the indications for its use have been extended.

Yonge in 1706 was the first who developed a suction cup. In 1849 Simpson reported "on a suction tractor, or a new mechanical power, as a substitute for the forceps in tedious labors". McCahey in 1890 called his instrument an "atmospheric tractor". In this century Torpin (1938), Koller (1950), Couzigou (1952) and Finderle (1955) have reported comparatively small series of deliveries with their instruments. But it was not until Malmström designed his instrument that a real interest was focussed upon the question.

For a detailed description of the instrument the reader is referred to Malmström's (1957) thesis (in English). The v.e. consists of a suction cup, traction chain and handle, a glass container with a vacuum gauge, and a pump. The different parts are connected by rubber tubes (Figs. 1 and 2).

The cup is made of metal and has the form of a capsule with a circular aperture to be placed upon the head of the foetus. The walls of the capsule are hemispherical, a form which reduces the tendency to slip when the artificial caput succedaneum fills out the cup. At one end the traction chain (also of metal) has a plate which directs the traction to the cup. The other end of the chain is passed through a rubber tube and connected to the traction handle with a washer. The glass container is fitted with a vacuum gauge and two metal connexions: one for a long rubber tube attached to the traction handle, and one for the tube to the suction pump. A valve in one of the connexions allows the vacuum to be decreased momentarily. Apart from the rubber tubes all parts are durable, and the instrument is easily assembled and sterilized. The cup is made in three different sizes, the aperture measuring 40, 50, and 60 mm. to adapt the instrument to the stages of dilatation of the os.

ANAESTHESIA

Malmström recommends a local infiltration anaesthesia in the perineum, if necessary completed with general analgesia when the instrument is introduced into the vagina. He does not use anaesthesia during delivery. According to our experience this can be modified slightly. We

find that a careful introduction of the cup causes no pain to the mother, so we infiltrate the perineum with xylocain while the vacuum is being obtained. If the mother does not co-operate much, we use a general analgesia when the head comes through. If wanted a general anaesthesia can be used in cases with low-lying head without danger to the child. The use of pudendal block has been reported.

Application of the Instrument

The mother is prepared as usual for obstetrical operation. A vaginal exploration is performed to decide the height and position of the head and the size of the os. The size of the cup is then chosen, preferably the largest possible. Should the os not be sufficiently dilated to permit the smallest cup to pass, it is often possible to dilate it with the fingers. Cervical incisions are not recommended. The cup is moistened, for instance in a sterile soap solution. It is then introduced into the vagina in the sagittal plane and pressed lightly against the head of the foetus. The site of application should preferably be the vertex, but in an abnormal presentation this is not always possible. If there is a preformed caput succedaneum this is the place to choose. When the cup is in position and in good contact with the head, a vacuum is to be created. This is done gradually, starting with 0·1 to 0·2 kg./cm.^{2} and increasing by 0·1 to 0·2 kg./cm.^{2} at intervals of 1–3 minutes until finally a vacuum of 0·7 kg./cm.^{2} has been reached. In cases where it is necessary to obtain delivery as quickly as possible, the final vacuum can be obtained in a couple of minutes without any damage to the child. Usually we increase the vacuum gradually, spending 5 to 6 minutes in all.

Delivery

The purpose is to help the natural mechanism of labour. This is done by intermittent traction synchronized with the pains. If there are only weak contractions of the uterus they will usually be increased even by moderate traction. Heavy traction should be avoided if the os is not fully dilated, since a cervical rupture might then occur. The direction of the traction is in accordance with the curve of the passage. If the v.e. is used instead of a low forceps the mother's labour is unnecessary, and the child can be delivered by traction alone.

Several authors have used light, but uninterrupted traction for a longer interval of time. We have no personal experience with this method.

Complications

As mentioned above the os usually can be dilated with the fingers, if it does not permit the smallest cup to be introduced. While the vacuum is produced the os has a tendency to be absorbed and to be jammed under the rim of the cup, but this can be avoided if a finger is passed along the circumference at regular intervals. By too heavy traction the perineum may be lacerated or the cervix ruptured if the os is not completely dilated, but with a little practice this can easily be avoided. The suction cup may slip if the direction of traction deviates too much from the curve of the passage, but it can be put into place again without damage. The risk of contamination of the passage seems to be slight. The artificial caput succedaneum normally disappears during the first 24 to 48 hours. Cephalhaematoma, small necrotic areas in the scalp or localized alopecia may result occasionally. The question of intracranial haemorrhage will be discussed later.

Review of Literature

As one could expect there is quite a number of different opinions on the conditions and indications for the use of v.e., but all authors agree upon certain points. The os must be sufficiently dilated to permit introduction of the smallest cup, and cervical incisions should be avoided. There must not be a foeto-pelvic disproportion of any importance, and the membranes must have been ruptured. Furthermore most authors claim that the head must be presenting, but Evelbauer (1956, 1958a, b) and Berggren (1958) have both applied the v.e. in a breech presentation. In cases of face presentation vacuum-extraction is not to be used. Rossel and Champod (1958) claim it to be dangerous for the child if the cup is placed over the large fontanelle, and for this reason they only apply the

FIG. 1

Shows from above the traction chain, the suction cup connected by a rubber tube to the traction handle, and below the instrument assembled.

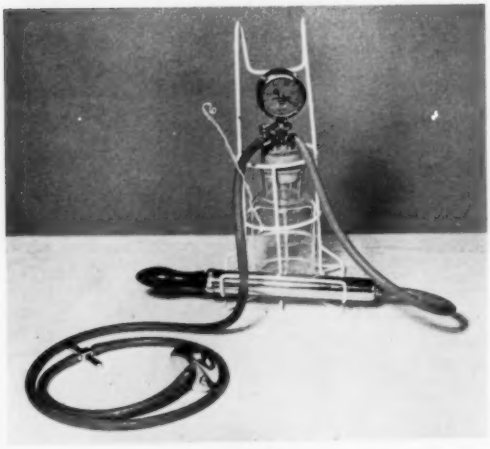

FIG. 2

Shows the vacuum-extractor connected to glass container and pump. The pump and the glass container need not be sterilized.

FIG. 3

Shows the superficial abrasion of the scalp in the anterior part of the artificial caput succedaneum.

FIG. 4

Shows the abrasion covered with a crust 6 days after vacuum-extraction. There is no disfigurement. The lesion healed without a scar.

v.e. in occiput anterior positions. According to Fürstenberg and Söderhjelm (1960) the large fontanelle should be avoided if possible, but not absolutely; Evelbauer (1958a), who has presented the largest series, and Berggren (1958) consider the question unimportant. Rossel and Champod (1958) use v.e. only in cases where the head is almost against the perineum, while Fauvet and Scheele (1956), Meinrenken and Schieferstein (1957), Barben (1958), Berggren (1958) and Evelbauer (1958) all find that the v.e. is particularly useful in cases where the head is in the mid-pelvic or even higher position. The rotation of the head is of minor importance since it usually follows spontaneously during traction upon a not fully rotated head. Some authors claim it possible to force rotation by rotating the cup.

According to most authors the main indications for vacuum-extraction are uterine inertia and threatening intra-uterine asphyxia, but experience has shown that the v.e. is excellent in replacing a low forceps. The indications have been widened to include occiput posterior and brow presentation, deep transverse arrest, funnel pelvis, prolapse of the cord, partial or marginal placenta praevia, abruptio placentae and high perineum. Evelbauer (1958a) and Berggren (1958) find that the v.e. can replace the forceps in most cases, while others are more reserved. Meinrenken and Schieferstein (1957) use forceps in all cases where the head is deflected, and, as already mentioned, Rossel and Champod (1958) limit the use of the v.e. to occiput anterior positions with the head lying low. The v.e. cannot be applied to the head when this is coming last.

Six large series of vacuum extraction have been reported (Meinrenken and Schieferstein, 1957; Barben, 1958; Berggren, 1958; Evelbauer, 1958a; Rossel and Champod, 1958; Lauridsen, Laursen and Fürstenberg, 1960), a total of 406 cases.

There were 2 maternal deaths, but neither was due to vacuum-extraction (Berggren (1958), one case of acute liver necrosis of the mother before extraction; Meinrenken and Schieferstein (1957), one case of aplastic syndrome (leucosis ?)). In 13 cases there was laceration of the perineum and in 7 cases laceration of the vagina. In 6 cases there was cystopyelitis, in 4 bleeding caused by uterine atony, in 3 cases endometritis, in 3 cases rupture of cervix or cervical incision, and finally, superficial phlebitis and atony of the bladder in one case each.

Eleven children were stillborn, but 7 of them were dead before vacuum-extraction. Of the remaining, one large baby (4,860 g.) died while the shoulder was being delivered, one died during delivery, according to the authors (Meinrenken and Schieferstein, 1957) probably because the cord was twisted twice round the neck of the child, and finally 2 died from intracranial bleeding (Berggren, 1958). One child was born alive but died later from intracranial bleeding (described in detail by Fürstenberg and Söderhjelm, 1960).

It has not been proved that the v.e. has caused intracranial bleeding, but the possibility cannot be excluded. In a few cases Fürstenberg and Söderhjelm (1960) have found an abnormally high number of erythrocytes in liquor spinalis from children delivered by vacuum-extraction. On the contrary they report autopsy of a child that died from congenital deformities a few hours after delivery. There was a subcutaneous haematoma in the scalp where the suction cup had been applied, but there was no intracranial lesion or bleeding.

Thirty children had cephalhaematoma or superficial abrasion of the scalp. One had a short period of tendency to cramps and one to cyanosis.

Aschan and Saloheimo (1953) have reported two cases of alopecia.

Evelbauer (1958a) examined 100 children one year after vacuum-extraction and found normal mental and physical development in all cases.

It is the general impression that most authors find the v.e. to be a valuable obstetrical instrument, particularly in cases where the head is rather high and the os is not fully dilated.

Author's Cases

Since 1st July, 1959, the v.e. has been in use in this department. In all cases the technique recommended by Malmström (1957) has been used: a vacuum of 0·7 kg./cm.^{2} and intermittent traction.

Episiotomy has been performed according to routine under local infiltration in the perineum with xylocain, and a short analgesia with chloroform; vinydan or trilene was given while the head came through.

There has been no mortality among mothers and children, and no case of asphyxia.

Eight of the mothers were 1-para, one was 2-para (the first child delivered by forceps), and one was 3-para (one of the former children delivered by forceps). The ages varied between 17 and 32 years.

Indications:

(1) Inertia uteri secundaria in 7 cases. In 4 of these it was the sole indication. In the remaining the additional indications were: toxicosis, one case; pulmonary tuberculosis, one case; and asphyxia intra-uterina imminens, one case.

(2) Posterior asynclitism arrested in the mid-pelvic plane: one case.

(3) Abruptio placentae praecox: one case.

(4) Lack of co-operation from mother: one case.

The duration of the labour varied from 5 to 62 hours, the average being 21 hours.

The os was completely dilated in 8 cases, and was estimated as 6 cm. in two cases.

In two cases the head was at the height of the spines, in the remaining it was close to or on the pelvic floor.

In 5 cases the head was fully rotated. In 3 cases it was in L.O.A.–L.O. 45 degrees, in one case in L.O.T.–L.O. 90 degrees. During traction these cases rotated to the occiput anterior position. In one case the head was in R.O.P.–R.O. 135 degrees and it rotated to the occiput posterior position.

The time of extraction varied between 4 and 20 minutes. In the 8 cases with low-lying head the average time of extraction was 6 minutes.

Nine children were delivered in the occiput anterior position and one in the occiput posterior position.

The weight of the children varied between 2,850 g. and 4,000 g., an average 3,345 g.

In all cases the episiotomy healed by first intention. In one case there was a minor laceration in an old episiotomy scar, but the healing was uncomplicated.

Eight mothers had a normal puerperium and were dismissed between the 7th and 10th days.

One mother had atony of the bladder of 4-days duration, complicated with cystitis (but no fever). She was dismissed on the 9th day.

The placenta was removed manually in the case with toxicosis, and the puerperium was complicated with urinary infection, fever and albuminuria. She was dismissed on the 19th day.

Three children had complications, but none of them was serious: one child had a cephal-haematoma at the place where the suction cup was applied, and one had a cephalhaematoma at a distance of 3 cm. from the place of the cup. No treatment was necessary. One child had a superficial abrasion of the scalp (the cup slipped once during traction). It was treated with nebacetin powder and healed quickly and without scar (see Figures 3 and 4).

In one case the v.e. had to be replaced by forceps: 18-years-old 1-para with signs of asphyxia intra-uterina imminens. The os was fully dilated and the head two fingerbreadths from the pelvic floor. The exact rotation of the head could not be determined. The v.e. was applied and intermittent traction was started. After 20 minutes there was no progress, and forceps delivery was decided. This was difficult too, and the child was delivered in R.O.P.–R.O. 135 degrees. It was suffering from asphyxia, but it soon recovered. The weight was 2,750 g. X-ray examination post-partum showed a moderately contracted pelvis. (This case is not included in the series of 10 cases.)

Conclusion

The v.e. is excellent as a substitute for low forceps. Furthermore it makes it possible to intervene in cases where the head has not descended and the os is not fully dilated. The technique of its use is easy to learn, but, since it may cause complications, the indications for its use must be very clear.

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CHORIONEPITHELIOMA IN MOTHER AND CHILD

BY

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CHORIONEPITHELIOMA is a rare tumour. Hertig and Mansell (1956) indicate a frequency of 1 in 40,000 pregnancies. The tumour is particularly seen following a molar pregnancy. An overall survey of all cases of chorionepithelioma shows, however, that 20–25 per cent of cases occur after a full-term or almost full-term pregnancy.

Chorionepithelioma is a tumour which arises from the trophoblast. Whereas previously the trophoblast was often regarded as a tissue with its own specific characteristics—not to be included either among the maternal or among the foetal tissues—the present trend is in favour of regarding the trophoblast as foetal tissue. Levy (1955) found that the sex-chromatin pattern in the trophoblast corresponds with the foetal sex. This holds true for the trophoblast of the normal placenta. This congruence is also found in cases in which the maternal chorionepithelioma can be correlated with near-certainty with a preceding pregnancy (Oosterhuis and Levy, 1957). Willis (1948) refers to chorionepithelioma as a "unique tumour, being of one individual transferred to another—a foetal tumour affecting the mother".

It is remarkable that chorionepithelioma does produce metastases in the mother but is believed not to metastasize in the child. In reviews of large series of cases—e.g., that of Park and Lees (1950) (502 patients)—no mention is ever made of chorionepithelioma in the child. Novak and Novak (1958) and Smalbraak (1957) also fail to mention this possibility, Wieberdink (1950), discussing the spread of malignant processes to the child *in utero* in his book on metastasization, does mention the possibility of chorionepitheliomatous metastases in the child. In *The Borderland of Embryology and Pathology* (1958), Willis also discusses this possibility, although he had no knowledge of established cases. In 1952 Emery described a neonate who, 48 days old, died of a haemorrhagic hepatic tumour with pulmonary metastases. Microscopic examination of the tumour revealed the features of a chorionepithelioma. The mother showed no anomalies even on gonadotrophin investigation. No such investigation was made in the case of the child. The hormonal activity of the tumour was manifested by hyperplasia of the Leydig cells in the testicles; these cells constituted one-fourth of the total testicular tissue. Leydig cells are readily recognizable in neonates during the first few weeks. However, Emery had never observed so marked a hyperplasia in his investigation of 300 infantile testicles. Animal experiments have shown that injection of pregnant urine causes an increase in the Leydig cell count in immature rats (Engle, 1929). In his publication, Emery touches on the possibility that the child's tumour might be a metastasis of the (maternal) chorionepithelioma.

The first case of chorionepithelioma in mother

and child was described by Bucknell and Owen in 1954. The child was born at term and, aged 7 weeks, died of a hepatic tumour with pulmonary and costal metastases after progressive anaemia. The mother was curetted for haemorrhage 9 weeks post-partum and a tumour with a diameter of 10 mm. was found in the right uterine angle.

The tumour of the child and that in the uterus showed identical features, corresponding to an anaplastic tumour such as chorionepithelioma. The mother remained well after hysterectomy.

The second case of chorionepithelioma in mother and child was described in 1958 by Mercer, Lammert, Anderson and Hazard. The child was born at term and, 3 days old, was treated for a haemorrhagic tumour of the alveolar margin of the maxilla. The microscopic structure of this tumour corresponded to that of a chorionepithelioma. Extirpation of the tumour was followed by a disappearance of the gonadotrophins found in the urine in high concentration. Nine days later, however, gonadotrophins were again encountered. The tumour recurred. The child died at the age of 7 months. No autopsy was possible.

The mother showed increasing haemorrhage during 8 weeks following parturition. Curettage then revealed a uterine chorionepithelioma. The maternal urine likewise contained gonadotrophins. These disappeared after total extirpation. X-rays revealed pulmonary metastases 3½ months post-partum. The test for urinary gonadotrophins at the same time reverted to positive. The woman died some 6 months after parturition. There was no post-mortem.

These cases from the literature show that chorionepithelioma can give rise to metastases not only in the mother but also in the child. They also show that, in view of the pronounced anaplastic nature of the tumour, the morphologist can hardly do without the support of hormonal investigation. A remarkable feature of the last-mentioned case was that mother and child died almost simultaneously.

The following facts are available with regard to the mother in our case.

The Mother

The menarche occurred at the early age of 9 years. The maternal grandmother died early of a malignant growth.

On 15th April, 1958, this 21-year old primipara was delivered spontaneously at term in the patient's home, supervised by the family doctor. The woman bled considerably before the placenta was finally delivered by the Credé manœuvre. The afterbirth seemed complete and showed nothing unusual.

The woman continued to bleed after this; shock ensued, and she was admitted to the Roman Catholic Hospital, Woerden. She received a transfusion of 1,500 ml. of blood, after which the general condition rapidly improved; the haemorrhage was arrested. On 19th April, the haemoglobin concentration was 8·6 g./100 ml., and another transfusion of 500 ml. blood was given. The puerperium remained otherwise uneventful. Breast feeding was sufficient, and the child seemed normal.

On 5th May, the woman was re-admitted with marked haemorrhage from the uterus. The uterus was still the size of a fist; the cervix admitted a finger. Two placental specimens of 2×2×1 cm. were found adherent to the right lateral uterine wall and were digitally removed. Histological examination (Dr. J. Zeldenrust) revealed no chorionepithelioma in these specimens, which consisted of placental tissue and decidua exhibiting inflammation. The bleeding had ceased when the patient was discharged on 12th May.

She was re-admitted on 17th September—5 months post-partum. She had a 3-day history of intermittent abdominal pain, particularly in the umbilical region. When walking, moreover, she had a sensation as if "a growth was moving" in the abdomen. During the past few months she had menstruated every 2–5 weeks. There had been slight pyrexia during the last few days before admission.

In the lower abdomen, a tumour was palpable rising to the umbilicus; the growth was tender. Vaginal digital examination showed that the uterus was not enlarged; it was retroverted. A large round, taut and cystic tumour filled the entire true pelvis and was continuous with the neoplasm palpable from the outside. During bi-manual examination this large tumour suddenly seemed less well defined and the woman complained of violent abdominal pain. The tumour was presumed to have ruptured as a result of the examination, and an immediate laparotomy was consequently performed.

There was a relatively large quantity of blood in the abdominal cavity; the uterus and the left adnexa seemed normal; the right ovary was transformed into a cystic tumour the size of a child's head. It had a thin membranous wall which showed a large tear on the anterior side. A large part of the contents had escaped into the abdomen. It consisted of a violet-reddish, fragile tissue interspersed by lighter red tissue trabeculae. The distal half of the omentum contained a similar tumour mass continuous with the ovarian growth. The proximal part of the omentum was normal and contained no visible or palpable metastases. Nor were metastases found elsewhere in the abdomen.

The ovarian tumour and the omentum were extirpated, while the uterus and the left adnexa were left *in situ*.

Microscopic examination (Dr. J. Zeldenrust): "Very extensive necrosis and occasional areas of neoplastic

tissue showing marked polymorphism and numerous syncytial elements with several mitoses. Very likely chorionepithelioma, although no Langhans' cells are visible."

On 23rd September, 6 days after the operation, the gonadotrophin test (Aschheim-Zondek) was negative. Curettage was carried out a few days later. No neoplastic tissue was found in the material curetted. There were dilated glands with inconsiderable secretion and some islets of metaplastic pavement-cell epithelium.

The post-operative course was uneventful. The patient received 25 mg. stilboestrol 4 times daily. The thoracic X-ray showed no metastases. The patient was discharged on 4th October.

Re-admission followed on 31st October, with symptoms of ileus. A large mass was palpable in the abdomen. Laparotomy revealed numerous metastases, particularly in the lower abdomen, but also in the liver and the omentum. Pathological examination (Dr. J. Zeldenrust) revealed chorionepitheliomatous tissue; Langhans' cells were also observed.

The urine contained gonadotrophins. These were not demonstrable, however, in diluted urine (1:50 and 1:100).

The temperature remained high after the operation (about 39° C.). There was ascites necessitating several punctures which always released blood-tinged fluid. Despite daily blood transfusion it was impossible to raise the haemoglobin concentration to above 8 g./100 ml.

Several blue-discoloured peri-umbilical tumours developed in the abdominal wall.

After consultation with the internist (Dr. R. G. A. van Wayjen), therapy by intravenous infusions of methotrexate was instituted, but a few days later death occurred (23rd November, 1958). Post-mortem examination was not permitted.

The Child

The child—a girl spontaneously born at term on 15th April, 1958 (birth weight almost 3,000 g.)—showed no anomalies during the first few months. She was breast-fed until age 5 months, when the mother was hospitalized for chorionepithelioma. She had since become less lively, and drinking had become less satisfactory (this was initially ascribed to weaning). At the same time, however, the child became increasingly pale and on 31st October she was admitted—simultaneously with the mother—in a markedly anaemic condition. The haemoglobin level was so low that it could not be recorded on the family doctor's facilities for determination.

The child's nutritional condition was still very good: body weight 8,800 g. She was still cheerful and active but showed a greenish-pale complexion. The skin was healthy, and there was no glandular swelling. The lung contours were very high but the lungs showed no radiological changes. The abdomen was slightly distended. A firm tumour was palpable (not tender) in the upper abdomen; the sharp lower margin of the growth extended as far as the true pelvis. This growth was chiefly localized to the left of the umbilicus. On the right the hepatic margin was palpable 2–3 cm. underneath the costal arch. The mammae were slightly swollen; the external genitals were normal. There were no cutaneous haemorrhages.

Syphilis and tuberculin tests were negative. The haemoglobin concentration was between 2 and 3 g./100 ml. Erythrocyte count 1,100,000; reticulocytes 150 per mille.

The thrombocytes and the white blood picture were normal. The bone marrow showed very marked erythropoiesis but no other anomalies.

There was nothing to support the theory of acquired or congenital haemolytic anaemia. Both the direct and the indirect Coombs tests were negative, Professor van Loghem's laboratory was unable to demonstrate haemolysins. The total blood bilirubin concentration was 0·9 U. Globular fragility: incipient haemolysis at 0·46 per cent NaCl; total haemolysis at 0·30 per cent NaCl. The serum-iron value was exceedingly low: 0·02 mg./100 ml., with a saturation percentage of 6.

The various findings indicated that this marked anaemia resulted from a haemorrhage which, however, was not demonstrable. The faecal benzidine reaction was repeatedly negative. Blood in the urine was never found.

The simultaneous existence of a tumour in mother and child raised the suspicion of an identical condition. Urinary gonadotrophins were consequently determined. The first determination was negative, probably because the sample was too small. A second determination using 24-hour urine was positive (Aschheim and Zondek).

The child was given a blood transfusion and the haemoglobin concentration rose to 9·5 g./100 ml. This increase, however, almost completely disappeared within a few days. The patient developed pyrexia up to 40° C., for which no infectious cause was demonstrated, although the leucocyte count increased to ·25,000. Antibiotics (penicillin and tetracycline) were ineffective. The abdominal volume rapidly increased, partly because of developing ascites, and partly as a result of rapid growth of the tumour, particularly to the right. It seemed likely that the neoplasm originated from the left lobe of the liver. Blue discoloration was seen around the protruding umbilicus. A naevus-like spot—about 0·5 cm. in diameter—was seen 6 cm. below the umbilicus.

On 30th November, the child was transferred to the Sophia Children's Hospital, Rotterdam (Dr. H. Reerink) for further observation. Gonadotrophin reactions were again carried out, with positive results on two occasions (according to Konsuloff and Galli Mainini).

The haemoglobin concentration had again markedly decreased, and it was not until after many transfusions that the child's condition was such as to permit of an exploratory laparotomy (26th November) to establish whether the tumour was still operable, sacrificing the left liver lobe if necessary. A large part of the abdominal cavity was found occupied by the liver, which was the seat of a tumour mass. The condition was completely inoperable. The biopsy specimen contained a polymorphocellular tumour with Langhans' cells and giant

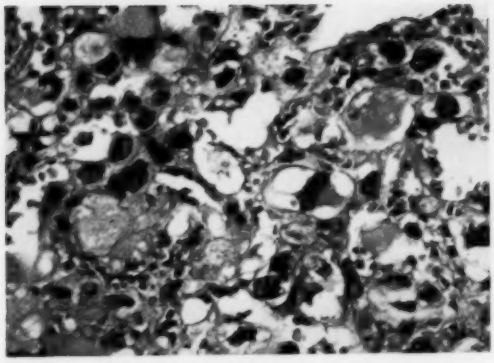

FIG. 1

Child. Liver biopsy specimen: anaplastic chorion-epithelioma. Haematoxylin-azophloxine staining. ×340.

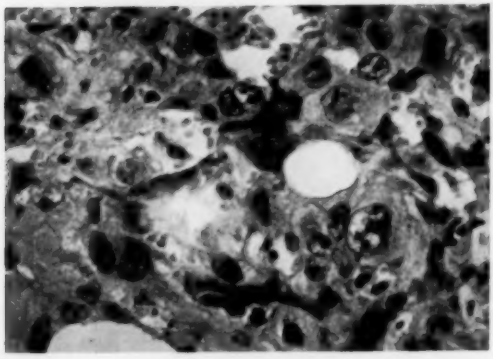

FIG. 2

Mother. Omental biopsy specimen: anaplastic chorion-epithelioma. Haematoxylin-azophloxine staining. ×340.

FIG. 4

Child. Abdomen opened showing enlarged liver.

FIG. 3

Child. Liver: horizontal section. Massive chorionepithelioma spread in the left half of the liver; boundary line at site of blood supply to left and right half of the liver.

cells, considerable haemorrhage and necrosis. The diagnosis was: chorionepithelioma.

Since the literature reports cures in 30 per cent of cases of chorionepithelioma treated with methotrexate (Hertz *et al.*, 1958), this treatment was instituted shortly after the transfer to Rotterdam. The daily dose was 2·5 mg., subsequently increased to 3·25 mg. No result whatever was seen. No toxic effects occurred.

Further treatment could be only palliative. The greatest difficulty was to maintain a reasonable haemoglobin concentration, despite almost daily transfusions. The half-value time of the erythrocytes, determined with the aid of radioactive chromium, was found to be only 3 days, and was therefore greatly accelerated. A jaundice which was partly haemolytic developed (total blood bilirubin value 12 U., one-minute percentage 42). Blood was occasionally found in the stools shortly before death.

The child became increasingly cachectic, and died on 13th December, 1958.

An autopsy was performed 20 hours post-mortem. The adipose layer of the thorax and the abdomen was only 0·2 cm. thick. The skin was bronze-coloured, with moderate jaundice. The linea alba was not pigmented; the mammae were slightly swollen, and the areolae not pigmented. No abnormal hair-growth was seen.

The abdomen was greatly distended. The skin showed a few peri-umbilical bluish-red spots, up to 4×2·5 cm. in size. As the abdominal cavity was opened, 80 ml. of blood-tinged fluid escaped. The peritoneum showed blood-filled tumours up to 2 cm. in diameter, invading the abdominal muscles and the skin. The externally visible blue discolorations were caused by these tumours. The omentum was locally adherent to the liver. The adhesions were readily severed.

The left half of the liver showed marked enlargement and extended in the median line and the right mamillary line as far as 25 cm. below the costal margin. This part of the liver, and the adjacent region of the right lobe as far as 3 cm. to the right of the falciform ligament, showed many grape-size, violet-red bulging soft tumours, between which no normal hepatic tissue was recognizable. The sections showed a corresponding picture.

The left branch of the portal vein was constricted by tumour tissue. The intima was intact, and no thrombi were found.

A sharp demarcation was seen 3 cm. to the right of the falciform ligament. To the right of this boundary the liver was not enlarged and showed a normal aspect. The colour was brownish-red; the liver configuration was just recognizable, and the substance was firm. The section also showed a normal pattern; the course of the portal vein was readily recognizable but the intra-hepatic bile passages were invisible. There was, however, an occasional encapsulated red node with a diameter of 0·5 cm.

The bluish-red tumour tissue locally shimmered through the cystic duct; the mucosa was intact. Under the intact mucosa of the duodenum, too, tumour tissue was visible in line with the lesser curvature, at about 1·4 cm. distance. The hepatic veins were normal.

The very large liver (weight 2,280 g.) had caused downward displacement of the intestines. The other abdominal organs were normal. The adrenals, pancreas, spleen and kidneys were free of macroscopic changes; the internal genital organs were of normal size. A follicle with a diameter of 0·3 cm. was found in the left ovary. The lymph glands along the aorta were dark red.

Among the cervical and thoracic organs, the thyroid was small, while the thymus was small, red and limp. The heart was normal. In the lungs—in the lingula of the left upper lobe at the boundary of the apex, and in the apex of the right upper lobe—a few encapsulated, firm nodules were found, with a diameter of 0·6 cm. and with a red cut surface.

No bone metastases were seen; a cranial autopsy was not granted.

Microscopic examination revealed chorionepithelioma in the liver, lungs, subcutaneous layers and adrenal glands. The structure corresponded with that found in the liver biopsy examined on 26th November. Comparison also showed that this structure was identical to that found in the mother in biopsy specimens from metastases obtained at the second laparotomy (31st October).

The microscopic structure of the organs of internal secretion, thyroid, pancreas and ovaries, was normal. The ovaries contained primordial follicles and central proliferation of the theca interna. Our experience is that this is a normal finding at this age, although comparative material is very scanty.

The mammae contained wide glandular ducts in hyalinized fibrous tissue; this finding is

probably not normal at this age. The uterus and cervix showed no anomalies; there was a congenital ectropion of the vaginal cervix. A striking feature was that the vaginal epithelium was not atrophic but comparable, in thickness and structure, with the epithelium found in neonates during the first week of life.

Summarizing it can be stated that mother and child showed an identical, anaplastic haemorrhagic tumour. Langhans' and syncytial cells were distinguishable in both growths. Both had a positive test for urinary gonadotrophin excretion. It is remarkable that, in the child, this hormonal function was morphologically manifested only in the mammae and in the vagina. Another striking fact is that this tumour became manifest in mother and child after the same interval post-partum (about 5 months), and led to a fatal issue in both cases about 8 months post-partum.

Discussion

Chorionepithelioma in mother and child is a remarkable condition, if only by the very rarity of its occurrence. Apart from this, the case described confirms the theoretical possibility of metastasization of a placental tumour (trophoblast) in mother and child (Wieberdink, 1950; Willis, 1958). Unfortunately, no cases have so far been described in which the placenta was also completely examined. The question remains as to whether such an examination would indeed reveal placental changes. In verified chorionepithelioma in the mother after a completed pregnancy, this is certainly not always the case (de Snoo, 1931, and others).

Among cases of chorionepithelioma in the child hitherto studied there is none in which this could be suspected immediately post-partum. The older literature (e.g., Friedreich, 1866) comprises reports on haemorrhagic anaplastic hepatic tumours in neonates, which showed marked microscopic similarity to chorionepithelioma. It remains possible, therefore, that chorionepithelioma in the child may occur without maternal metastases, as was probably the case in the observation of Emery (1952). The morphological diagnosis can be made more definite only by gonadotrophin determination.

It is possible that a primary chorionepithelioma developed in the child before birth. Arguments against this possibility are—apart from the interval post-partum—localization in the liver and particularly a localization as encountered in our case. *In our case, tumour tissue was almost exclusively found in the left half of the liver—i.e., an area corresponding with the circulatory region of the umbilical vein in the liver during the intra-uterine period.*

The pathogenesis of chorionepithelioma is a controversial subject. Among the factors mentioned as important are general maternal disorders (absence of antibodies against the trophoblast), ovarian anomalies (insufficiency or dysfunction), disturbances in the ovum itself (inclusion of male gametocyte) and local disturbances in a part of the ovum, i.e., the trophoblast.

The embryologist Hertig and his colleagues (1940, 1947) focussed particular attention on the similarity in structure and behaviour between the very young ovum (7 days) and the trophoblast of some moles. In the case of a morphological similarity, according to Hertig, the chance of similar behaviour—i.e., uninhibited infiltrative growth (with metastasization)—would be considerably greater. Smalbraak (1957) was unable to confirm this in his material.

Hertig's theory is very attractive in the case of chorionepithelioma in mother and child. Assuming that the trophoblast locally retains the characteristics found in the very young ovum, there are no theoretical difficulties in explaining the infiltrative growth and the metastatic growth. The remarkable similarity in the time of manifestation of the metastases in mother and child, and in the time of death, can then be explained without difficulty.

There remain a few points which, in our case, require attention. The mother started to menstruate as early as age 9. No data are available which indicate that this early menarche was based on an ovarian tumour. The localization of the chorionepithelioma in the right ovary, however, might suggest a primary tumour in this ovary, with metastasization in mother and child. Although this could not be excluded with certainty, it is improbable in view of the rarity of primary chorionepithelioma in the

ovary. Mother-ovum metastasization of other malignant processes, such as lymphosarcomatosis, Hodgkin's disease and malignant melanoma, has been described (Buckell and Owen, 1954). No such description is available regarding primary chorionepithelioma.

In the mother, curettage revealed no tumour in the uterus. Hertig and Sheldon (1947) pointed out that, in patients who developed chorionepithelioma following a molar pregnancy, this was strikingly seldom revealed at examination of the *entire uterus*. Novak and Koff (1930) state with regard to chorionepithelioma: "A considerable group of cases is recorded in which the uterus has completely thrown off the chorio-carcinoma."

Park and Lees (1950), moreover, report ovarian metastases in 6 per cent of choriocarcinomata (16 out of 263 cases). According to these publications, metastatic chorionepithelioma in the ovary in the absence of a uterine tumour (not demonstrable in our case) can very well arise from the trophoblast.

A final remarkable feature was that, in the child, the gonadotrophic effect of the chorionepithelioma had not become morphologically manifest, although urinary gonadotrophin excretion existed. However, a lactotrophic action was morphologically likely. The vagina exhibited changes due to oestrogenic influences (adrenals?, ovaries?).

Summary

A description is given of a case of chorionepithelioma in mother and child. The possibility of metastasization of this tumour in both has been confirmed by this new case (the third in the literature). The tumour showed identical macroscopic and microscopic features in mother and child. The hormonal gonadotrophic function was also found to be identical.

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NEW ZEALAND'S DEBT TO BRITISH OBSTETRICS*

BY

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IT was with a deep sense of honour, Mr. President, that I received the invitation to give the William Meredith Fletcher Shaw Memorial Lecture for 1960, and the pleasure was the greater in that its founder, that grand elder-statesman of the College in Great Britain, has also been a very great friend and wise counsellor to us, in New Zealand. It was the recollection of Sir William's important services to us, and the fact that this year was the first occasion on which a New Zealand Fellow has been given the signal distinction of appointment as a Sims-Black Travelling Professor, that turned my thoughts to the debt we owe to British Obstetrics in so many various ways as an appropriate subject for my address. And if the impressions which I try to convey are coloured by personal experiences, I think that you will understand.

That debt goes back a very long way. Its beginning, indeed, lies in our common heritage from great pioneers like William Smellie and J. Y. Simpson and the Chamberlens. There is a sentimental streak in some of us in New Zealand, too, that has watched with warm approval the steps which have been taken in recent years to preserve and record more adequately the relics of these honoured figures in obstetrical history. Already well familiar with their stories, it has been one of my pleasant privileges to make pilgrimage to the present-day repositories of these treasures of the past.

Then in the first 50 or 60 years of the development of our country New Zealand was entirely dependent on Britain for medical personnel and even when the Medical School was founded in the latter part of last century there were few facilities for the training of medical students in obstetrics. Nor was there any midwifery nursing training school until 1904. As a consequence New Zealand women were much more dependent on the family doctor for attendance at confinement than was the case in Britain.

For this reason many of our young doctors-to-be, realizing the responsibilities that they would have to face, still elected to train in Great Britain and to gain some proficiency in this work in one or another of the big maternity institutions, not only during their undergraduate training but often also in resident posts before return. And so there grew up a tradition of self-reliant and capable general practitioner obstetricians which continues to be a feature of our service.

Such was my own experience in Edinburgh as one of the last of those who went overseas almost as a matter of course, for the period 1911 to 1915, and then sought postgraduate refreshment after the war and before return. Looking back on it all, how valuable it was to have spent some weeks in residence at the Rotunda Hospital in early 1915 during the Joint-Mastership and to have come under the influence of greatly respected seniors like Sir William Smyly and Dr. R. D. Puerfoy, and particularly, Dr. Hastings Tweedy, already known throughout the world for his outstanding results in eclampsia treatment. With them as Assistant Masters were R. E. Tottenham and E. C. Crichton, who later carried the banner of British Obstetrics to Hong Kong and South Africa respectively. And what an opportunity it was to return to a resident appointment at the old Simpson Memorial Hospital in Edinburgh in 1919 first as Sir Halliday Croom's last houseman and then under J. W. Ballantyne at the time when he was just

* The William Meredith Fletcher Shaw Memorial Lecture, 23rd September, 1960.

beginning his pioneer antenatal work. Contacts were made, too, with James Young and F. J. Browne just preparing to take their prominent places in modern obstetrics. That is but one example of the experiences that came the way of many New Zealanders, which inspired in them an interest in this work, gave them confidence in it and, unconsciously perhaps at the time, shaped their future careers. Many of us of that generation think with gratitude of those influences.

After the 1914–18 War so many of the New Zealand trained graduates had also visited Britain while on service that there was a much wider awareness of simmering changes in obstetrical practice and of the increasing importance of overseas contacts. Undergraduate training in New Zealand was now firmly established, with a general standard which was highly regarded, but obstetrics remained the Cinderella department without a chair. The teaching was in the hands of a part-time lecturer, raised to the status of Professor in 1929. To remedy matters, those with special interest in obstetrical practice now formed an active Obstetrical Society. We now turned more to Britain for assistance at the postgraduate level, and not only did many of the Otago graduates seek such experience, but several of Britain's leading obstetricians and gynaecologists generously accepted the invitation of the Society to lecture throughout the Dominion and assist us with our administrative problems. This you will understand was before the foundation of the College. I wonder if you who have the constant stimulus of contact with many highly qualified colleagues can fully appreciate the eagerness with which our small groups hailed those visits?

Perhaps the highlight of those early lecture tours was Mr. Victor Bonney's visit. Already known to many by his postgraduate teaching in London, by his brilliant operative technique and by his lucid writings, he gave himself with enthusiasm to this new type of peripatetic teaching and helped us greatly by his powerful advocacy before Government and university authorities in our big project of the moment, the establishment of the Chair of Obstetrics and Gynaecology at Dunedin, which was finally achieved in 1931 when Professor Bernard Dawson (later Sir Bernard) received the first appointment and began that long and successful period of constructive service which built up the Department of Obstetrics and Gynaecology in the Otago University to a position of world-wide respect.

Following his visit Mr. Bonney maintained a keen interest in our country, gave invaluable help to many of our young graduates and put an indelible stamp on more than one of our now leading specialists.

Mr. Bright Bannister was another distinguished colleague from whose visit we derived much pleasure and profit.

With the foundation of the College in 1929 a new era in postgraduate training, with the Membership as its hallmark, began. In this great advance New Zealand shared and now, in a more systematic way, our young graduates, aiming at specialization, were generously assisted to obtain the necessary practical and theoretical instruction in the two branches of the combined specialty.

Again, some of us of the older generation, remembering the relatively limited facilities that were available to us, much as we appreciated them in our day, think with gratitude of the sound basic training that is now available to our sons and daughters as the result of the insistence of the College on this high, and essentially practical standard.

The growing influence of the College has also helped us greatly in the next essential step, the gradual development of combined obstetrical and gynaecological units in all the major hospitals. This, of course, is the firm policy of the College and it is absolutely necessary that, as the fully trained men become available, as is now the case, the major New Zealand hospitals shall fall into line if they are to be acceptable to the College for the provision of some of the training for the Membership Examination. The development of the obstetrical departments has been relatively easy but the combination with gynaecology has met in some directions with the same opposition which faced you in many of your hospitals a generation earlier. It was the more understandable too in our country since, as I have explained, the fully trained specialist

only began to appear on the scene less than 30 years ago and gynaecological surgery in our hospitals was firmly in the hands of very competent general surgeons.

But gradually the Hospital Boards and the Health Department, which has a controlling financial interest in hospital appointments, are being convinced that this step is essential for the early postgraduate training of many of our young doctors who find it difficult to spend all that training period abroad, and also to attract back to our country the men with the high skills provided by the full membership course. Furthermore, if they lag behind, the standard of practice in these hospitals will inevitably suffer.

In 1946 Sir William Fletcher Shaw came to New Zealand at the invitation of the New Zealand Obstetrical and Gynaecological Society with the primary purpose of advising on matters concerning the establishment of a postgraduate obstetrical and gynaecological hospital in Auckland and the appointment of the first Professor to the newly-endowed Chair of Postgraduate Obstetrics and Gynaecology. He also spent 3 months with us studying the wider problems in the evolution of our obstetrical and gynaecological services. His report to the Government was received with great respect by the authorities and much of his advice has been followed. He continued to watch our interests with a fatherly eye and his name will ever be honoured in the annals of New Zealand obstetrical history.

Another milestone in our progress was when our College representative body was raised to the status of a Regional Council. The official inauguration was performed by Sir William Gilliatt in 1951 at a most dignified and impressive ceremony which focussed attention on our growing specialty. Since that time we have had many evidences of the consideration given by Council to the New Zealand point of view and a warm welcome has been given to representatives of the Regional Council and other Fellows and Members when visiting Britain. I cannot let this opportunity pass without expressing our sincerest thanks for the generous place that was given to New Zealand on the recent most important occasion of the official opening of the splendid new College building which we all hope will, more than ever, be the focal point of Commonwealth obstetrical relationships.

I have spoken earlier of the great benefit that we all derived from the visits of senior colleagues from Britain arranged by our Obstetrical and Gynaecological Society. These have continued and the Society has seized on every opportunity presented by the presence of such men on postgraduate teaching assignments in Australia, or latterly at our own postgraduate school in Auckland, to extend their visits to include other centres in the country. Those invaluable contacts have also been ensured of greater frequency and regularity by the foundation in the College of the Sims-Black Travelling Professorships through the vision and great generosity of Sir Arthur and Lady Sims and their daughter Mrs. Margaret Black, to whom we extend our deepest appreciation. In this way we have had the stimulus that reading alone does not give by eager discussion with Mr. G. F. Gibberd, Sir Andrew Claye and Mr. J. B. Blaikley as Sims-Black Travelling Professors and with Sir William Gilliatt, Professor Gilbert Strachan, Sir Arthur Gemmell, Professor F. J. Browne, Professor T. N. A. Jeffcoate, and Sir Andrew Claye on an earlier occasion, when they were in Australasia for other reasons. To all these men we are greatly indebted.

My thoughts turn next to the influence of British literature in the field of obstetrics and gynaecology. Although we are so far away from both Britain and the United States of America we are, in a way, strategically placed to benefit from the winds of opinion from both countries. We would be the first to acknowledge all that we have learnt from America but, in the main, it is to Britain that we still look for the balanced view in the approach to most of our problems. It has ever been the genius of all the best writing and teaching in Britain that it has so carefully held that balance between the conservative and the progressive. I can think of no better example of that than in the writings of that great teacher Professor Munro Kerr over the years.

And how has obstetrical practice in New Zealand fared under this tutelage? Professor B. P. Watson when delivering this same memorial lecture in 1955 spoke of the healthy

sharing of knowledge in striving to teach a common goal and said, "One country with better facilities for the exploitation of some new clinical or scientific fact, often originating in another, may have gone ahead more quickly with its practical application, but it has never been long before the rest have caught up". We like to think that we have been apt pupils and that by reason of our small and homogeneous population, the general high standard of living which has been our fortunate lot, and our possibly more closely integrated medical and nursing services, we have contributed something to the common pool by quicker demonstration of the possibilities of combined preventive action. Following up that thought it is interesting to trace the way in which that has happened in several fields.

The Attack on Puerperal Sepsis

In the early nineteen twenties the New Zealand maternity service was under a cloud because of the high maternal mortality rate in the country, with puerperal sepsis as the leading cause. We were not alone in that position but in a small country the people are perhaps more quickly shocked by an episode such as an outbreak of sepsis in a small maternity hospital.

There were several important reports of investigations made in Great Britain which helped us, but actually it was a rugged country practitioner, Dr. T. L. Paget, with an intense conviction that this thing could be beaten by meticulous attention to the simple details of a standard aseptic and antiseptic technique, which could be applied even in the country homes in which he was accustomed to work, who led the attack. He was given a co-ordinating position in the Health Department as Inspector of Maternity Hospitals, and with the keen assistance of the newly-formed Obstetrical Society things soon began to happen. Dr. Henry Jellett, ex-master of the Rotunda Hospital, who was in those years consultant obstetrician to the Department of Health in New Zealand, also exercised an important influence on the development of the maternity service.

By 1936 we were considerably nearer the ultimate goal than either Great Britain or the United States. Our puerperal sepsis death rate following childbirth, which had been 2·1 per 1,000 livebirths in the 1921–25 period, had been reduced to 0·36 per 1,000 in 1936. The corresponding figures for Britain were 1·8 to 1·18, and for the United States from 2·7 to 2·3. In 1936 we were helped still further by a great technical contribution on the part of Dr. Leonard Colebrook and his associates at Queen Charlotte's Hospital. Incidentally it was with very great pleasure that we welcomed Dr. and Mrs. Colebrook at an Australasian Congress in Dunedin a few years ago and heard his own reminiscences of those early days.

Then came the sulphonamides, and if the original discovery did not come from Britain, British chemists were soon in the forefront in the development of improved members of this group. And, of course, it was not long before we were sharing the great benefits of the discovery and therapeutic application of penicillin by Sir Alexander Fleming and Sir Howard Florey. But in these days of concern about the extensive development of bacterial resistance against antibiotics is there not something to be learnt from that early New Zealand experience to which I have referred? Having got so far on the road to puerperal sepsis control without sulphonamides or antibiotics, our need for them in the final stages of the campaign, much as we valued them, was much less than was the case in those countries which had had less success and now saw in these drugs the real solution of their problem. May it not be that a second look at the details of present day aseptic and antiseptic techniques, as actually being carried out, might be one of the ways to reduce the call on antibiotics? In saying this I am thinking more of our current outstanding problem—nursery infection—rather than of puerperal sepsis.

Toxaemia Control

Toxaemia control is another field in which I think that we can fairly claim that we have applied accumulated knowledge, much of which derived from Britain, with quicker response than many.

I have already mentioned my early associations with J. W. Ballantyne and F. J. Browne.

Those contacts had left me with a deep conviction of the possibilities of antenatal care, particularly in toxaemia prevention, and that enthusiasm was shared by all the active members of our young Obstetrical Society. These reminiscences of co-operation between the mother country and our growing Dominion would not be complete without a reference at this point to the late Dr. Doris Gordon, the virtual founder of the Society and its vital secretary for many years, for whom this link became a passion and who, already a Fellow, was honoured as a great ambassador by the College with the rare distinction of an Honorary Fellowship.

And so it was that toxaemia became one of our priorities. With the very great advantage of eclampsia notification for over 30 years we have been able to follow progress step by step. I have on more than one occasion developed that theme while in this country and will not go into the subject in any detail; suffice it to say that while general progress was at first disappointingly slow, the convincing demonstration of most encouraging results in certain areas where preventive measures had obviously been more thoroughly applied, gradually won the effective co-operation of all those engaged in obstetrical practice. An outstanding memory of those early days is of the interest and the challenge which came from the splendid results which were obtained by Dr. Oxley and his nursing team working in this field in the humble surroundings of the East London Hospital.

During all those years we could offer little in the way of laboratory research but we were in a position to examine critically all the evidence that had gradually accumulated and to base our practice step by step on a correlation of what to us appeared to be the most significant clinical points. If we presume to discuss these questions with those who have long had the facilities for organized research, which are only now being developed in our country, it is on the strength of the leading position which again we were able to take in preventive action on a national scale.

Treatment of the Haemorrhages

Turning now to the haemorrhages and thinking first of post-partum haemorrhage, many of the outstanding contributions to its control have come from Britain. We do not forget that pituitary extract was first introduced to obstetrics in 1908 by William Blair-Bell, the first President of the College. It is my impression that some of us in New Zealand exploited its great advantage more widely and with greater success than was the case elsewhere. Recognizing the grossly wrong uses and the excessive dosage which in some cases led to serious trouble and brought pituitary extract into undeserved suspicion, we found an invaluable place for it not only in the treatment of post-partum haemorrhage but also preventively in the third stage at a time when it was the only potent quick-acting ecbolic available.

To Britain, too, we are indebted for the even more vitally important discovery of ergometrine which came to us through the research work and clinical trials of Dudley and Chassar Moir. It was with particular pleasure that several New Zealanders were able to share in the tribute paid to Professor Chassar Moir on the recent occasion of the presentation to him of the first Eardley Holland Gold Medal for his part in this great contribution to medicine.

Here again, I think that it would be fair to claim that New Zealand has made one notable contribution to the prevention and control of post-partum haemorrhage by demonstrating the advantages of hospital confinement in all cases. We believe that there are so many quite unpredictable emergencies—post-partum haemorrhage probably the most important of them—that this is the safest course. Under such conditions these invaluable agents which we have been discussing, and the supplementary steps in treatment which may be necessary, can be used much more quickly and effectively.

The gradual development of the modern assessment and treatment of ante-partum haemorrhages has been the work of many, but Professor Macafee's part in convincingly demonstrating the possibilities of a watchful policy—in hospital—in many cases of placenta praevia, rather than immediate delivery, a direction in which many others were gropingly feeling, stands out as another of the outstanding advances in obstetrical practice.

Treatment of Difficult Labour

In no direction perhaps have we looked more to Britain for the balanced view—progressive but not extravagant—than in the assessment and treatment of disproportion and malpresentation. I think again particularly of the influence of great clinicians like Munro Kerr with his vast experience of the problem in the days when Caesarean section had very little place in the treatment who then guided us with careful judgment in our approach to the new developments of radiological investigation and the wider use of Caesarean section, now made possible by the great advances in sepsis prevention and surgical technique.

Those outstanding early studies of Eardley Holland into the causes of stillbirth, too, had a very important influence on breech management in New Zealand. In later years we have learnt much more in breech delivery, particularly from the Liverpool school.

In the closely associated problem of inefficient uterine action it is the clear thinking of British obstetricians like Jeffcoate which has crystallized for many of us in New Zealand our own very similar ideas on this subject.

Infant Wastage

In the solution of the problem of first year infant wastage, that most important joint responsibility of obstetrician and paediatrician, New Zealand is justly recognized to have taken an early lead, but there again there have been many developments for which we have Britain to thank.

As early as the 1900 period all three components, stillbirths, neonatal deaths and 1 to 12 months deaths, were considerably lower than in Britain and, indeed, were amongst the lowest in the world. That this was so in spite of the fact that we could not claim any superior scientific knowledge may seem very surprising, but in retrospect it is now perfectly clear that this was due to our relatively high standard of living. Unconsciously perhaps, New Zealand had produced clear evidence of the primary importance of those social and economic factors which in more recent years have been so exhaustively and scientifically studied, especially by Sir Dugald Baird.

In the second decade of this century the striking success of Sir Truby King's system of preventive care in the 1 to 12 month period, which quickly became a feature of New Zealand national life, soon led to the application of many of its salient principles to the neonatal period, with further improvement. In particular, deaths from infection originating in the neonatal period were practically eliminated and new principles in the care of the premature baby saved many lives.

It is in the more technical and scientific approaches to the other aspects of perinatal mortality that we have learnt so much from Britain. Mention has already been made of the great advances in the reduction of the hazards—to both mother and infant—of haemorrhage, difficult labour and toxaemia. To these can be added many other contributions in the paediatric field.

Here again we have a striking illustration of B. P. Watson's observation concerning the ultimate equalizing effect of shared knowledge; gradually the position in our two countries is becoming closely parallel.

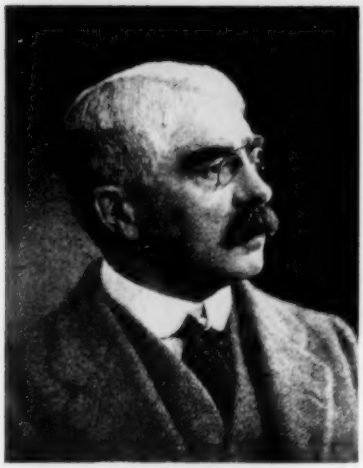
Mention must also be made of the opportunities that have been made possible for a not inconsiderable number of our colleagues to find advancement in this branch of medicine, as in other fields, in directions quite impossible in our small country. Many of those ex-patriates have attained positions of professional eminence and have done much to strengthen still further the bond between us. Our thoughts turn with particular pride and affection to the late Sir Charles Read who achieved the great distinction of election as President of our College and whose too-early death during his period of office and at the height of his career was such a sad loss to us all. For him the fostering of this Commonwealth link was a matter of deep concern.

And what of the future? As far as New Zealand is concerned, Britain still holds the pre-eminent position in our regard as firmly as ever. But we must face the fact that the pre-eminence is meeting strong challenge in some Commonwealth areas from other countries in which medical science is surging ahead, backed by great resources in equipment.

It has been my great privilege during my tenure of the Sims-Black appointment to see

much exciting original work being undertaken and much farsighted planning in university departments and hospitals. The younger generation of obstetricians and gynaecologists has an eager, scientific, questing spirit associated with a great tradition of sound practice. Well may they say in words very similar to those once used in another field of national endeavour—"Give us the tools and we will maintain British supremacy". It is our earnest hope that those in a position to do so—in the Health Service and in the ranks of private benefactors who see in this a matter of national importance—will give them full backing.

A. DONALD



W. E. FOTHERGILL

NOTICE

of a

DONALD AND FOTHERGILL MEETING

to be held at

SAINT MARY'S HOSPITALS, WHITWORTH PARK, MANCHESTER

on

FRIDAY, 7TH JULY, 1961

comprising a symposium on the subject of

UTERO-VAGINAL PROLAPSE

under the aegis of

THE NORTH OF ENGLAND OBSTETRICAL AND GYNAECOLOGICAL SOCIETY

IT is now some fifty years since Archibald Donald and William Edward Fothergill, Honorary Surgeons at Saint Mary's Hospitals, worked at the same time on the problem of the surgical cure of utero-vaginal prolapse. Donald's approach was largely by clinical and operative trial, as befitted the dedicated clinician and indefatigable operator (1908–1921). Fothergill, on the other hand, worked from a basis of anatomical research (1907), and subsequent operative application (1913–1921) in deference to his scientific and artistic mind.

The result, as the world of gynaecology knows, is the operation which is variously called the "Manchester" or "Fothergill" operation, and one which perhaps has come to be as widely practised throughout the world (albeit with individual modifications), as any other standard operative procedure.

In consideration of these facts, we feel that it would be appropriate at this time to hold a meeting at Saint Mary's Hospitals, in order not only to pay a tribute to these distinguished men, and the reputation which they bequeathed to the Manchester school, but also to revise in the light of our added experience, our own views on this subject and its various facets.

The meeting itself, informal in nature, will benefit from the presence of any gynaecologist in the country who is able to attend. Discussion upon the scientific aspects of this so common and important condition, an operating session to cover three or four cases of differing type by surgeons who would offer to demonstrate their methods of colporrhaphy, and short papers to be read and discussed would fill in the time of the meeting, which would be solely concerned with the condition of utero-vaginal prolapse.

Gynaecologists who would wish to attend this meeting are asked to communicate with Dr. K. V. Bailey, Saint Mary's Hospitals, Whitworth Park, Manchester 13, not later than 31st March, 1961.

BOOK REVIEWS

"Diuresis and Diuretics." An International Symposium. Chairman, H. SCHWIEGK. Edited by E. BUCHBORN and K. D. BOCK. Pp. xii+382, with 88 illustrations. Springer-Verlag, Berlin, 1959. Price D.M. 25.50.

THIS volume contains a complete report of the proceedings of a symposium entitled "Diuresis and Diuretics" held in Herrenchiemsee from 17th–20th June, 1959, and which was sponsored by CIBA A.G., Basel. There were 39 participants from Austria, Germany, Switzerland, the United States of America and Professor Sheila Sherlock from London, who presented a review of the use of diuretics in liver disease.

Reviews and the ensuing discussions concerning the present state of knowledge of the mechanism of diuresis and the physiology and pharmacology of diuretic drugs were presented and are printed in full (a few of them are in English). Clinical reviews, in addition to that mentioned above, were devoted to the anti-hypertensive effects of diuretics and their use in heart disease, renal disease and in obstetric practice. V. Friedberg, Mainz, presented the latter review, which included a discussion of the causes of water retention in normal pregnancy and in pre-eclamptic toxaemia. Mercurial diuretics were shown to have the greatest effect on the water and salt retention occurring during pregnancy and carbonic anhydrase inhibitors the least, whilst hydrochlorothiazide occupied an intermediate place. Hydrochlorothiazide was considered to be the most suitable diuretic for use in pregnancy because it could be used for maintenance therapy once the oedema had resolved in response to initial treatment. The failure of diuretics in severe toxaemia was ascribed to hypervolaemia and haemoconcentration.

Peter J. Huntingford

"Moderne Entwicklungen auf dem Gestagengebiet. Hormone in der Veterinärmedizin." The 6th Symposium of the German Society for Endocrinology. Edited by H. NOWAKOWSKI. Pp. viii+441, with 276 illustrations. Springer-Verlag, Berlin, 1960. Price D.M. 96.

THE 6th symposium of the German Society for Endocrinology was held in Kiel from 28th–30th April, 1959. It was mainly devoted to a consideration of recent advances in the development and application of progestational substances, and to hormones in veterinary medicine. The papers presented, apart from one in English and one in French, were read in German, and they and the discussions which were provoked by them are printed in this volume.

The symposium was opened by a review of the chemistry and the effects of progestational substances and this was followed by a review of the metabolism of naturally occurring progesterone, and another concerning the use of radioactive isotopes for the investigation of progesterone metabolism during pregnancy. Original contributions included a comparison of the effects of progestational substances in ovariectomized women; the effects of nortestosterone on the hypothalamus and the hypophysis; the antagonism of progesterone and ethinyl nortestosterone; the influence of 6α-methyl-17α-acetoxyprogesterone on female sexual functions; the cytostatic effects of progestational substances; and the effects of progestogens and their metabolites on the basal temperature. This part of the symposium was concluded by reviews of the experimental basis of progesterone therapy; depot therapy with progestogens; and one by Swyer concerning the problems involved in the clinical evaluation of progestational steroids.

Other papers on a wide variety of endocrinological topics included contributions on the metabolism of androgens in the ovary; the intra-nasal use of oxytocin in the management of lactation; and the relationship between gonadotrophin output from the hypophysis and the hypothalamus.

Peter J. Huntingford

"Public Health and Social Services." Fifth edition. By the late DENNIS GEFFEN, *O.B.E.*, M.D., D.P.H., L. FARRER BROWN, *C.B.E.*, B.Sc., and MICHAEL D. WARREN, M.D., D.P.H., D.I.H. Pp. 164. Edward Arnold (Publishers) Ltd., London, 1960. Price 10*s.* 6*d.*

THIS, as described in the Preface, is "an elementary textbook describing the health and social legislation and services in this country". In 24 short chapters it outlines the nature and function of the various bodies, statutory and voluntary, that are concerned with the vast and complex mechanism of the Welfare State: Central Government, local authorities, National Health Service, Maternity Services, Care of Children, mental health, etc. It brings up to date in this, the fifth edition, the services relating to care of children as embodied in the Children's Act, 1959, the Adoption Act, 1958, the Legitimacy Act, 1959 and the changes in the Local Government Act, 1958 and the Housing Act, 1957. It is a handbook that should be in the hands of doctors, nurses and health visitors as well as lay officers charged with the day to day administration of social and health services.

"Anaerobic Bacteriology in Clinical Medicine." By A. TREVOR WILLIS. Pp. xii+163, with 13 figures. Butterworth and Co., London, 1960. Price 30*s.*

ANAEROBES are much neglected in diagnostic bacteriology except in wartime when special teams of bacteriologists are trained for the rapid diagnosis of clostridial infection. This is a pity because at least one-third of closed

abdominal and genital abscesses yield anaerobes and when antibiotic treatment is required it should be aimed at all potential pathogens. Dr. Trevor Willis is to be congratulated on writing a book which will help clinical bacteriologists in this field.

Techniques of anaerobic culture and essential tests for identification are clearly set out and for those who are interested there is an extensive bibliography for further reading.

My only criticism is that, in the section on anaerobic infections, more weight is given to clostridial infection than its frequency in civilian practice justifies. This, however, is inevitable because so little is known at present about the non-sporing anaerobes which are so much more frequently encountered. In his foreword Professor Oakley pleads for interest in the "non-pathogenic" anaerobes. The female genital tract is full of them and it seems likely that some, now believed harmless, will prove pathogenic when more is known about them.

The book is well set out, easy to read, and its price is reasonable. It should prove invaluable to clinical bacteriologists and of interest to all those faced with the problem of the diagnosis and treatment of deep-seated purulent infections.

E. Joan Stokes

"Encyclopaedia of Urology." Edited by C. E. ALKEN, V. W. DIX, H. M. WEYRAUCH and E. WILDBOLZ. Springer Verlag, Berlin, 1960.

Vol. III. "Symptomatology and Examination of the Blood, Urine and Genital Secretions." With contributions by KARL HINSBERG (Düsseldorf), JOSEF KIMMIG (Hamburg), JOHANNES MEYER-ROHN (Hamburg), R. H. O. B. ROBINSON (London), CARL SCHIRREN (Hamburg) and RENATE WEHRMANN (Hamburg). Pp. xvi+337, with 61 illustrations. Price D.M. 118.

VOLUME III begins with a chapter by R. H. O. B. Robinson, in English, on abnormalities of urine volume and composition. The remaining chapters are all in German. They contain detailed descriptions of the methods used for investigating the constituents of urine, blood and prostatic secretions. Physical, chemical and bacteriological techniques are described as well as the methods for detecting antibiotics in blood and urine and the assay of steroid hormones. The value of the various tests is also critically discussed. There is a brief but useful section on the examination of semen and the laboratory assessment of male fertility. This book contains a wealth of information; it is a compact reference manual to the technical details of many laboratory investigations, which are used daily in every branch of medicine. The index refers to the English and German texts in alphabetical order and in the appropriate language; the editors are to be congratulated on its compilation.

Vol. IX/2. "Inflammation II—Specific Inflammations." With contributions by EINAR LJUNGGREN (Göteborg), R. CAMPBELL BEGG (Johannesburg) and AMBROSE J. KING (London). Pp. xvi+564, with 90 illustrations. Price D.M. 158.

THE whole of this volume is written in English. It contains detailed descriptions of the pathology, clinical picture and treatment of tuberculosis and parasitic infestations of the genito-urinary tract, syphilis, lymphogranuloma venereum, granuloma inguinale and chancroid. The chapters on tuberculosis and venereal diseases review the subjects completely (there are 20 pages of references concerning genito-urinary tuberculosis). The sections on the diagnosis and treatment of these diseases are particularly useful to the gynaecologist, who may occasionally be faced with a diagnostic problem and be required to understand the modern treatment of these conditions. Tuberculosis of the female genital tract is not described. The descriptions of the multitude of parasitic affections of the genito-urinary system are fascinating, even if of little practical significance to the European practitioner, but their inclusion is justified by the encyclopaedic nature of the work.

Vol. XII. "Functional Disturbances." With contributions by A. AUERBACK (San Francisco), C. E. BURKLAND (Sacramento), G. W. PARADE (Neustadt), J. C. ROSS (Liverpool), D. R. SMITH (San Francisco) and W. W. WILLIAMS (Springfield). Pp. xiv+312, with 74 illustrations. Price D.M. 98.

FOUR of the contributions to this volume are in English and one in German (the chapter on tetany). There are two chapters that will be of interest to the gynaecologist; one deals with functional disturbances of the bladder and impotence in the male, and the other deals in detail with the investigation and treatment of male sterility. This last chapter also discusses the problem of artificial insemination. The remaining contributions are devoted to urogenital allergy and to neuromuscular dysfunction of the bladder and paraplegia, providing a practical guide to the management of these unhappy patients.

These three volumes are beautifully printed and bound, and the quality of the illustrations is excellent. Inevitably in a work of this nature there is considerable repetition, but this does ensure that the Encyclopaedia is comprehensive. The reader is not continually disturbed and referred to other contributors or worse still to other volumes, because each chapter is complete in itself.

Peter J. Huntingford

"Fortschritte der Geburtshilfe und Gynäkologie." Vol. II. Edited by A. REIST. "The Problem of Toxoplasmosis." With contributions by W. ROTH and JOSEF A. ČECH and OTTO JÍROVEC. Pp. iv+90, with 10 figures. S. Karger, Basel and New York, 1960. Price Sw. Fr. 17.70.

THE first part of this monograph deals with the laboratory diagnosis of toxoplasmosis. The difficulties of isolating and detecting the organism are described in detail, as are the serological reactions that have been used to provide evidence of a past or present infection, The author has found that the combination of the Sabin-Feldman dye test and the complement-fixation reaction gives the most reliable information for clinical purposes. The clinical

significance of the laboratory results is discussed in detail and the chapter concludes with a consideration of the epidemiology of toxoplasmosis.

Čech and Jírovec, working in Prague, have investigated the importance of latent maternal infections with toxoplasmosis. From 1954–1956, 379 women, who had become pregnant after a previous miscarriage, stillbirth, premature labour or having had a congenitally malformed infant, were investigated to detect the presence of infection with toxoplasmosis. In 233 of these patients the intra-dermal test with toxoplasmin was positive. From this and other observations the authors conclude that latent maternal toxoplasmosis may not only produce the classical neonatal syndrome, but it may also cause recurrent abortions, intra-uterine death and possibly other minor illnesses in the newborn infant, such as jaundice and pneumonia. Fifty women with latent toxoplasmosis, who had had repeated abortions or stillbirths, were treated with pyrimethamine. In the pregnancies prior to treatment 96 per cent of the foetuses died, whereas after treatment only 16 per cent of the infants died. The point of view expressed by these authors contrasts strongly with that of Roth who considers that a foetus is only likely to be affected if the mother acquires toxoplasmosis during the pregnancy.

The first contribution is in German and the second in English. The latter is sometimes difficult to follow. The two contributions show how difficult it is to interpret the significance of latent maternal toxoplasmosis. Quite apart from the confused writing and presentation of the second chapter, the problem remains unsolved.

Peter J. Huntingford

"Atlas der Gynäkologischen Anatomie." (Atlas of Gynaecological Anatomy.) By HEINRICH MARTIUS and KÄTHE DROYSEN. Pp. viii+118, with 134 illustrations. Georg Thieme, Stuttgart, 1960. Price D.M. 49.

HEINRICH MARTIUS, the distinguished German gynaecologist whose name has been connected with the University of Göttingen for many years, has written several obstetric and gynaecological textbooks and surgical treatises. In preparation for these books numerous anatomical studies were undertaken by him and by Käthe Droysen, the gifted artist associated with him; it is these which form the bulk of the Atlas.

The introductory text is written in German, but the captions to the illustrations are in three languages: German, English and Spanish. As the book is obviously meant for international circulation, the authors wisely chose Latin names for the anatomical structures. P. J. Huntingford has supplied the translation of the legends for the English reader who can easily find his way through the interesting part of the volume: the illustrations of topographical anatomy, many of them coloured.

The authors did not intend the work to be of a systematic nature. They admit that some subjects have been dealt with generously, others briefly and some have been omitted altogether. Thus, there is no mention of the breast, or of the placenta, except for its early stages. Scant attention is given to the bladder, rectum and anal canal. In a book which is meant for the scientific and practising specialist in gynaecology and obstetrics, these gaps might usefully be filled in a future edition. One would have liked to see details of the ischio-rectal fossa and the relations of the vagina, as well as a full plate showing all the nerves supplying the vulva (not just the pudendal nerve). The bulbo-cavernosus muscle seems perhaps disproportionately large in several illustrations. There are minor errors such as the naming of "theca interna" and "externa" in Figures 87 and 88. It should be pointed out that the mesonephric duct in the male gives rise not only to the epididymis but also to the rete testis.

Many of the pictures are beautifully executed. The general design and the production of the book are in accordance with the high standard which one has learnt to expect from Georg Thieme publications.

Bruce Eton

"Medical, Surgical and Gynecological Complications of Pregnancy." Edited by A. F. GUTTMACHER, M.D., and J. J. ROVINSKY, M.D. Pp. x+619. Illustrated. Baillière, Tindall & Cox, Ltd., London, 1960. Price 132*s*.

IN the Obstetric Department of the Mount Sinai Hospital 10 specialty clinics have been established, namely cardiac, pulmonary, hypertensive-renal, diabetic, haematologic, neurologic, psychosomatic, obstetric-gynaecologic endocrine, vaginitis and varicose vein. Each of these clinics is directed by one of the senior staff of the specialty concerned, routine antenatal care being provided by the resident obstetric staff. Such an arrangement has stimulated in other specialists a particular interest in the pregnant woman and the information and experience so gained provide the basis of this book. The titles of the 14 sections range from cardiovascular-renal system to genetic considerations, from eye, ear, nose and throat to collagen disorders, and from dermatology and syphilis to malignancy. Some 70 contributors are listed and, as might be expected, the scope and quality of the various chapters vary greatly. Some, such as those on heart disease and tuberculosis, provide extensive reviews of the literature as well as a detailed description of the Mount Sinai policy of management. Other subjects are essentially reviews with comparatively little personal contribution. As the editors state in the preface, this volume is in no way intended to supplant the usual textbooks, but it should provide a very useful book of reference. Very few conditions in any field of medicine are not dealt with and the obstetrician faced with some rare associated disease should find this book of great value.

James G. Lawson

"The Reluctant Surgeon." By JOHN KOBLER. Heinemann, London, 1960. Price 21*s*.

IN this reconstruction of the lives and times of William and John Hunter, the former receives more of the early limelight but John is the hero of the title. Not intended primarily for medical readers, this biography is somewhat

journalistic in style and uneven in treatment, the background being often given undue prominence and extraneous events included for picturesque effect.

If, as the author states in his preface, "Hunter has not fared well at the hands of his biographers", this injustice has not yet been wholly remedied. Yet despite these qualifications, this book, like any other about the Hunters, must attract interest and attention, and the extensive bibliography shows that the author, who writes from Connecticut, U.S.A., must have done his research work very thoroughly.

S. Bender

"Obstetrics." Twelfth edition. Edited by J. P. GREENHILL. Pp. xiii+1098, with 903 figures. W. B. Saunders, Philadelphia and London, 1960. Price £5 19*s*.

THIS is a completely new edition of the late Dr. De Lee's renowned textbook, under the sole editorship of Dr. Greenhill. For the first time, other authorities (23 in all) contribute chapters on special subjects, including the physiology and biochemistry of the placenta, endocrinology, radiology, the toxaemias of pregnancy, and nutrition.

The book is very well produced, the illustrations are lavish and explicit, and the type clear, though the double-column layout so dear to the heart of the American publisher does not make for free reading. The references and the index are both exhaustive.

Many of the contributions are excellent, the chapter on the physiology of the placenta by Dr. Ernest Page being a concise, clear and thoroughly up-to-date summary of present knowledge on this complex subject. Erythroblastosis foetalis is also comprehensively dealt with, and the recommended management reasoned and logical.

There is still, however, undue emphasis on out-dated methods of treatment—there is a very full description of the method of using Champetier de Ribes' bag in the treatment of placenta praevia, though the author admits that he himself does not employ it. Interrupted injections of pitocin are still advocated in the induction of labour, and the dilute intravenous pitocin infusion given insufficient emphasis, the dangers being exaggerated.

The problem of postmaturity is very summarily dealt with. Dr. Greenhill does not believe that there is any danger to the foetus in postmaturity—this being his experience at the Chicago Lying-In Hospital—but produces no evidence to substantiate his contention. His suggestion that maturity can confidently be determined by the state of ripeness of the cervix ("if the cervix is closed, the patient is not at term regardless of how many days or weeks she has gone beyond the calculated delivery day") is most misleading, and potentially dangerous.

The sections on X-ray placentography and on uterine dysfunction are disappointingly inadequate. This is especially true of the second of these subjects, this chapter being very unsystematic in layout: the management of these cases is not well described.

With these reservations—and a second glance at the cost of the book, which is high by British standards—this work can be recommended as a well-produced and comprehensive account of modern obstetric practice.

THIRD WORLD CONGRESS OF THE INTERNATIONAL FEDERATION OF GYNAECOLOGY AND OBSTETRICS

THIS Congress will be held in Vienna from 3rd to 9th September, 1961.

The following subjects will be the chief topics of discussion:

(1) Surgical treatment in gynaecology and obstetrics
Conservative operations for fibroids; operations for stress incontinence; operations for aplasia vaginae; surgical treatment of carcinoma of the cervix; treatment of incompetent cervical os; forceps; vacuum extractor; treatment of breech presentation; anaesthetics in Caesarean section.

(2) The role of the pituitary gland in the physiology and pathology of genital organs
Diagnosis and treatment in Sheehan's disease; treatment with gonadotrophin in anovulatory cycles; induction of labour with pituitrin.

For further information apply to Doz. Dr. Grünberger, Scientific Secretary, Alserstrasse 4, Vienna IX, Austria.

REVIEW OF CURRENT LITERATURE

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PREGNANCY

1. Pregnancy in the Woman Over Forty.

By A. L. HIGDON. *Amer. J. Obstet. Gynec.*, **80,** 38–42, July 1960. 13 tables. 7 refs.

Among 21,818 mothers delivered in the 9 years 1950–58, 522 (2·44 per cent) were over 40 years of age. Of these 6 per cent were primiparas. There was no increase in duration of labour, prematurity, placenta praevia, or accidental or post-partum haemorrhage, but mid-forceps deliveries and Caesarean sections were more frequent. Mongoloids were 2 per cent. The author considers that the dangers of pregnancy in elderly women are "perhaps exaggerated". *F. J. Browne*

2. Alterations in Liver Function During Normal Pregnancy.

By R. D. MCNAIR and R. V. JAYNES. *Amer. J. Obstet. Gynec.*, **80,** 500–505, Sept. 1960. 4 tables. 18 refs.

This is a study of 600 normal pregnant women in order to determine the influence of normal pregnancy on liver function.

Cephalin cholesterol flocculation was found to be negative in 24 hours throughout pregnancy, though 8 to 12 per cent had a 2 plus or greater flocculation at or near term.

Thymol turbidity, which is a more sensitive indicator of homologous serum jaundice or infectious hepatitis than the other tests done, remains within the normal range, though a slight rise was observed, especially in the last trimester. In the first and second trimesters the average was 2·5 units. This increased in the last trimester to an average of 3·3 units at term, and there was a definite increase in the percentage of women with values above 5 units, beginning at the 7th month. In the third trimester 15 per cent had a thymol turbidity of over 5 units.

Total cholesterol starts to increase during the fourth month when the average was 160 mg. per cent and 9 per cent had values over 250. It continued to increase through the 8th month by which time 57 per cent had values above 250. Elevation of cholesterol is probably due to changes in steroid metabolism and may be considered normal in pregnancy.

Serum bilirubin values above 1 mg. per cent were observed in 24 of 564 women. No values of 2 mg. per cent were found nor any consistent differences in the monthly averages.

Total plasma protein concentration falls during pregnancy because of plasma dilution though the total amount of circulating protein is increased by 18 per cent. The *albumin globulin ratio* falls. During the third month the average was 2·1; the maximum decrease had occurred by the fifth month when the average was 1·7 which did not return to normal at the time of labour.

Alkaline phosphatase activity increased markedly in the third trimester when 42 per cent had values above the normal.

After delivery cephalin flocculation and thymol turbidity tests return rapidly to normal which suggests that the disturbances are not due to parenchymal cell damage but to obstruction of the liver or biliary tree as a result of increased intra-abdominal pressure.

F. J. Browne

3. Alkaline Phosphatase in Human Liquor Amnii. (Ueber die alkalische Phosphatase im menschlichen Fruchtwasser.)

By W. MISCHEL. *Zbl. Gynäk.*, **82,** 1382–1386, Sept. 3, 1960. 1 table. 1 fig. 25 refs.

The author determined the concentration of alkaline phosphatase (AP) in liquor and in maternal and foetal plasma, using the method of King-Armstrong. The level in liquor varied between 2 and 55 King-Armstrong Units (KAU), with an average of 14 KAU per 100 ml. At the

time of birth the concentration of AP in liquor was higher than it was in maternal and foetal serum. The presence of meconium in liquor raises the AP considerably and figures up to 225 KAU were reported. At seven months of pregnancy the level was about the same as at term. There was no simple relation between the concentration in the maternal and in cord blood, nor between the level in the liquor and the length, weight or sex of the child.

The source of AP remains unknown. It used to be thought (Abderhalden) that the rise in the maternal AP level in pregnancy was secondary to foetal osteogenesis. It has, however, not yet been proved that the AP can pass the placental barrier.

The significance of the presence of the enzyme in liquor amnii is as little understood as is its origin.

Bruce Eton

4. Platelet Counts in Pregnancy and Labor.

By A. Mor, W. Yang, A. Schwarz and W. C. Jones. *Obstet. and Gynec.*, **16**, 338–343, Sept. 1960. 5 tables. 3 figs. 40 refs.

Platelet counts were done in 200 pregnant women in each trimester of pregnancy and in 250 patients during and after labour.

The results show a significant and continuous increase in the platelet count during pregnancy. The level remains constant in the first and second stages of labour but there is a precipitous drop in the platelet count coincident with the onset of placental detachment. The level rises again to normal in the post-partum period.

The greatest decline in the platelet count is seen in cases of severe post-partum haemorrhage and intra-uterine death.

J. G. Dumoulin

5. Na^{24} Uterine Muscle Clearance in Late Pregnancy.

By R. Landesman and R. C. Knapp. *Amer. J. Obstet. Gynec.*, **80**, 92–103, July 1960. 4 tables, 8 figs. 13 refs.

The authors investigated sodium^{24} uterine muscle clearance in 114 pregnant women. In normal pregnancy the half life clearance time was considered to be less than 6 minutes and clearance times above that were regarded as abnormal.

Of 23 patients with chronic hypertension 10 had abnormal clearances; in one patient with twin pregnancy and hypertension the time was extremely long. Of 13 patients with pre-eclampsia 6 had abnormally long clearance times and in one of these the time became longer as term approached, the hypertension having increased. The infant weighed 4,840 g. During sodium clearance in 5 patients concomitant sodium blood levels were obtained. It was found that there was a rapid increase in sodium levels which in normal women reached its maximum in 8 minutes after which it gradually decreased. This indicates a rapid taking up of the sodium by the blood. Five patients showed supine hypotension during the clearance, with giddiness and weakness and a fall of blood pressure as low as 60/30, associated with slow clearance. The condition is rectified by turning the patient on her side.

F. J. Browne

6. A Statistical Evaluation of the Cases of Eclampsia Treated in 72 German Hospitals in 1957 and 1958. (Auswertung der gemeinsamen Eklampsie-Statistik der Jahre 1957 und 1958 aus 72 deutschen Frauenkliniken.)

By H. Kyank and E. Schubert. *Geburtsh. u. Frauenheilk.*, **20**, 1038–1048, Sept. 1960. 19 tables.

Five hundred and twenty-seven cases of eclampsia (197 ante-partum, 174 intra-partum and 156 post-partum) treated in 1957 and 1958 have been collected from 72 German maternity hospitals. Seventy-six per cent of the patients were primigravidae and 90 per cent were nulliparous. In 69 cases (13 per cent) eclampsia occurred as a complication of toxaemia superimposed on essential hypertension. In 5 cases there was also abruptio placentae; in 1 case anuria; and 1 case was associated with a hydatidiform mole. Four hundred and fifteen of the patients were less than 30 years old. In 46·5 per cent of the cases the first fit occurred after admission to hospital. There were 22 maternal deaths (2 died undelivered), 4·17 per cent. Of the patients with eclampsia admitted to hospital before delivery 116 were delivered by Caesarean section and 5 of them died; 246 were delivered by more conservative methods, of whom 11 died.

The incidence of multiple pregnancy was 5·9 per cent, and a total of 557 infants were delivered. The incidence of congenital malformations was 2 per cent. The perinatal mortality rate was 19·3 per cent. One hundred and thirteen of those patients with an audible foetal heart on admission to hospital were delivered by Caesarean section and 15 (13·2 per cent) of these babies died; whereas 242 other cases with an audible foetal heart were treated conservatively and of these 53 (21·9 per cent) babies died (this difference is statistically significant.) The figures do not allow an evaluation of the different methods of treatment of eclampsia to be made.

[The only value of this large series of cases is to emphasize the maternal and foetal mortality rates associated with eclampsia, and to present the results of Caesarean section compared with more conservative methods of delivery. It is to be regretted that such a large series of cases of a relatively rare condition did not give an opportunity for assessment of the value of different methods of treatment of eclampsia.]

Peter J. Huntingford

7. The Results of Active Treatment of Fulminating Pre-eclampsia and Eclampsia. (Ergebnisse aktiver Behandlung der Präeklampsie und Eklampsie.)

By P. Dörffler. *Geburtsh. u. Frauenheilk.*, **20**, 1111–1123. Oct. 1960. 14 tables. 25 refs.

The author reports the results obtained in the University Gynaecological Clinic, Kiel, from 1938–1959, where it has been the policy to interfere actively and effect immediate delivery in cases of fulminating pre-eclampsia (increasing hypertension, albuminuria and oedema and/or associated with subjective symptoms) and eclampsia. One hundred and forty-five cases of fulminating pre-eclampsia and 189 cases of eclampsia were treated during this period; the Caesarean section rate for these 2 groups was 53 per cent and 65 per cent, respectively. Forceps delivery and breech extraction was performed in 29 per cent of the

total, whereas spontaneous delivery occurred in only 18 per cent of the total and in only 2 per cent of those with eclampsia. The results are compared in two consecutive periods from 1938–1948 and from 1949–1959. During these two periods 20 of 127 mothers (15·7 per cent) and 3 of 62 (4·8 per cent) died from eclampsia. The corresponding figures for fulminating pre-eclampsia were 3 maternal deaths in 89 cases (3·3 per cent) from 1938–1948; and from 1949–1959 there was 1 maternal death in 56 cases (1·8 per cent).

The perinatal loss associated with fulminating pre-eclampsia from 1938–1948 was 16 of 95 infants (17 per cent); from 1949–1959, 58 infants were delivered, 8 (13·9 per cent) of whom died. The perinatal loss from eclampsia was 21 of 140 infants (15 per cent) born between 1938–1948, and 8 of 69 infants (11·6 per cent) born between 1949–1959.

The author believes that these results, when compared with similar series, justify the continuation of the policy of active intervention by immediate delivery in cases of fulminating pre-eclampsia and eclampsia, particularly, as in recent years both the maternal and perinatal mortality rates have been reduced.

Peter J. Huntingford

8. **Haemodynamic Factors in Pre-eclampsia.** (Fattori emodinamici nella patologia ostetrica.)

By J. Bieniarz. *Minerva ginec. Torino.*, **12**, 807–813, Sept. 15, 1960. 4 tables. 5 figs. 23 refs.

This author's work on the venous and lymphatic drainage of the pregnant uterus is already well known, and in the present article he begins by pointing out that in cases of placenta praevia the three classical signs of pre-eclampsia (gestosis) are rarely observed, and similarly that gestosis is rarely accompanied by placenta praevia. This can scarcely be a coincidence. It is further to be observed that gestosis is more common in primigravidae, whilst ante-partum haemorrhage is commoner in multiparae. It would hence appear that low implantation of the placenta which conduces to ante-partum haemorrhage opposes the development of gestosis, and that the higher the placental insertion at the fundus the greater the chance of gestosis developing and the less probability of ante-partum haemorrhage.

There are two paths of venous and lymphatic drainage from the uterus, by the uterine and iliac route, and, in the opposite direction, by the ovarian veins and lymphatics towards the renal and portal systems. The flow of blood from the non-pregnant uterus is not considerable whilst from the utero-placental area it can reach up to a litre per minute, imposing a heavy strain on the haemodynamic system. If a large proportion of this blood and lymph takes the ovarian route a serious amount of back-pressure can be imposed upon the renal and portal veins. The proposition, that in cases of placenta praevia the blood drainage is predominantly to the uterine and iliac veins whereas when the placenta is developed at the fundus a large volume of blood finds its way back via the ovarian plexus, was submitted to test by observation conducted on 183 women delivered by Caesarean section (the indications for which were dystocia 73 cases, haemorrhage 56, gestosis 10, foetal distress 31, other 12).

Special attention was paid in each case to two points, first, the direction of the main venous flow as indicated by the prominence, dilatation, prominence and tortuosity of the veins, and, secondly, the position of implantation of the placenta, whether high, middle or low, front, back or lateral. It was found in the cases thus examined that all the vessels from the anterior aspect of the uterus and along the round ligaments drained downwards towards the uterine and iliac veins, tributaries of the inferior vena cava; only the most lateral were directed up towards the ovarian pampiniform plexus and so towards the renal and visceral venous systems. But, after delivery of the child, when by exteriorizing the uterus a complete view of its posterior aspect can be obtained, it is seen that blood from the fundus, and especially its posterior aspect, tends towards the ovarian system although the lower half drains to the uterine veins in the base of the broad ligament. The relative proportional amount of blood draining in these two opposite directions was then related to the observed position of insertion of the placenta and to the symptoms of pre-eclampsia or ante-partum haemorrhage if either was present.

Analyzing the results, eclampsia and gestosis were almost confined to cases where the placenta was developed at the fundus or upper part of the back of the uterus (and the higher the more probable effect), the blood passing via the ovarian veins; abruptio placentae to the mid-posterior or equivocal area of drainage, and no cases of gestosis were associated with low implantation so commonly accompanied by ante-partum haemorrhage (placenta praevia), where almost no blood from the placental area was judged as passing upwards.

[An additional factor predisposing in primigravidae to upward drainage is the greater pressure on the vena cava at the level of the pelvic brim due to more tense anterior abdominal walls.]

W. C. Spackman

9. **Gout and Pregnancy.**

By A. B. Weingold. *Obstet. and Gynec.*, **16**, 309–313, Sept. 1960. 19 refs.

Only 5 per cent of cases of gout occur in females, and the onset of the disease is usually post-menopausal. Gout associated with pregnancy is extremely rare and the author, who describes a case with tophaceous gout, was only able to find 3 other reported cases.

It seems that pregnancy is marked by remission of gouty symptoms, while the post-partum period is complicated by acute exacerbation. The author's case, who was followed through 2 pregnancies, had a blood uric acid of 10·5 mg. per cent but no toxaemia and only minimal nitrogen retention. In both pregnancies there was little trouble although after the first the baby died of hyaline membrane disease. The second baby showed a high blood uric acid at birth which was normal at 4 weeks. This is in contrast to other case reports of uraemic episodes in association with pregnancy.

J. G. Dumoulin

10. Results of Treatment in the Maternity Department of the Diabetic Institute, Karlsberg. (Beobachtungen auf der Entbindungsabteilung der Diabetikeranstalt im Karlsberg.)

By E. VON SCHUBERT. *Geburtsh. u. Frauenheilk.*, **20,** 1029–1037, Sept. 1960. 5 tables. 10 refs.

The author reports his impressions of a visit to the Karlsberg Institute for Diabetes. This hospital was founded by Dr. Katsch and is devoted to the treatment of diabetes mellitus; it has its own maternity department for the delivery of diabetic mothers, which is supervised by Dr. Worm. In 7 years (1952–1959) 376 diabetic mothers were delivered; 2 mothers died, 1 from postpartum eclampsia and 1 from a pulmonary embolus, both of them had been delivered by Caesarean section.

The perinatal mortality rate was 15·9 per cent (59 babies) and was composed as follows, 4·9 per cent died before the onset of labour, 2 per cent died during labour and 9 per cent died after birth. Nineteen (5·1 per cent) of the infants had gross congenital malformations.

There were two main methods of treatment; 127 patients were delivered by Caesarean section at 35 weeks and the perinatal mortality rate for this group was 20·5 per cent (26 infants), of which 7 died before delivery and there were 19 neonatal deaths. The remaining 249 women were treated by more than usually careful supervision of the diabetes and artificial rupture of the membranes at 37 weeks; 33 of these babies (13·2 per cent) died, 11 before the onset of labour, 7 during labour and 15 after birth. The majority in this group were delivered spontaneously.

[It is unfortunate that many valuable details are missing from this paper, particularly with regard to the fate of the patients treated by surgical induction. But by any standards the perinatal mortality rate associated with diabetes complicating pregnancy reported here is admirable and worthy of further attention. It is strange that a visitor should present the results of the clinic, but Dr. Worm has in fact written a monograph on this subject, *Diabetes und Schwangerschaft*, 1959, Abhandlungen der Deutschen Akademie der Wissenschaften, Berlin.]

Peter J. Huntingford

11. Follow-up Examination of Mothers of Out-sized Babies with Regard to Pre-Diabetes. (Nachuntersuchungen der Mütter übergrosser Kinder bezüglich Prädiabetes.)

By M. SZINNYAI and R. HUNKA. *Zbl. Gynäk.*, **82,** 1184–1189, July 30, 1960. 1 table. 17 refs.

A search for the pre-diabetic state should be made amongst women who have borne out-sized children, women who give a history of intra-uterine death, repeated miscarriages or premature labours, women suffering from obesity, those with a family history of diabetes, those who had children with congenital malformations and those with glycosuria in pregnancy.

The authors report their findings in a series of 346 mothers of out-sized children [presumably children weighing more than 4,500 g. at birth] delivered between 1946 and 1949. The obstetric history of these women included 873 pregnancies, but the incidence of premature births, intra-uterine deaths and congenital malformations was the same as in the other women delivered during the 4 years.

In 1958, i.e., 8–12 years after the delivery, the 346 women were requested to undergo further investigation. Seventy-three women attended. In 6 of these (8·2 per cent) the glucose tolerance test showed a raised, so-called pre-diabetic curve. The criteria of a pre-diabetic curve were a fasting blood sugar exceeding 120 mg. and rising above a peak of 200 mg. or remaining raised above 120 mg. at the end of the second hour. In 4 cases (5·4 per cent) an actual diabetic curve was observed.

A striking observation was that in the group suspected of pre-diabetes the incidence of toxaemia was twice and that of hydramnios three times as high as the general incidence.

Bruce Eton

12. Full-Term Extra-Uterine Pregnancy. (Voltydse ekstra-uterine swangerskap.)

By J. P. DU TOIT and J. N. DE VILLIERS. *S. Afr. med. J.*, **34,** 572–575, July 2, 1960. 5 figs. 10 refs.

The incidence of full-term extra-uterine pregnancy at the Karl Bremer Hospital, Bellville in a 34-month period was 1:1,134 cases. Four cases are described. In 2 the foetus had died prior to admission and one of these was septic. In 3 of the cases the placenta was removed. Right ureteric damage occurred in 1 patient.

Diagnostic features are discussed. Perhaps the most important feature was to consider the possibility of extra-uterine pregnancy. There is often a history of infertility or post-abortal sepsis. There may have been abdominal pain in early or late pregnancy. Postmaturity and death of the foetus before term are also important features. The foetus is often felt high up in the abdomen and foetal parts may be easily felt. The cervix is long and not taken up. It may be displaced. Sometimes the uterus can be felt apart from the foetus. Special investigations include straight X-ray of the abdomen, hysterogram and injection of pitocin to note whether the mass contracts.

Management is discussed. Early diagnosis and laparotomy will prevent foetal loss in many cases. The post-operative course is better when the placenta is removed. but this may be a dangerous procedure and adequate blood must be available. In some cases with partial separation removal becomes imperative.

L. J. Abramowitz

13. The Colpocytology of Postmaturity. (La colpocitologia della gravidanza oltra il termine.)

By P. E. BERTOLI. *Minerva ginec., Torino*, **12,** 733–737, Aug. 15, 1960. 6 plates. 1 table. 19 refs.

In distinguishing between physiological and pathological prolongation of pregnancy beyond the calculated (Naegele) date, various tests and criteria have been proposed. If the usual excess of 14 days is adopted, the child may be normal, macrosomic or pathologically postmature, etc. A colpocytological test that is at the same time simple and innocuous is described and illustrated,

and its readings compared with the clinical appearance of the delivered foetus. One hundred and ten women with deliveries overdue by at least 15 days were tested by examination of vaginal smears. Twenty-one of these were rejected as the smears were vitiated by trichomonal or other vaginitis. The remaining 89 were divided into three groups: (1) a group of 52 cases (58 per cent) where the foetus, placenta and liquor amnii were normal, (2) 24 cases (27 per cent) where although the foetus was normal the placenta and liquor showed characteristics which would indicate danger to the foetus, and (3) 13 others (15 per cent) where the foetus was clinically postmature or was stillborn and the placenta and liquor indicated postmaturity. Vaginal smears from the first group judged by the criteria applied indicated normal pregnancy at term or short of it (test negative). In the second group the slides indicated that the pregnancy was at or just beyond term. In the third group 23 per cent of the slides indicated full term and were thus false negatives, the rest indicated either mild or dangerous postmaturity (test positive). The test is therefore by no means specific, though there were no false positives. Positive slides showed absence of basophil cells desquamated in clumps but many eosinophil superficial cells with pyknotic nuclei. The article is illustrated with stained slides showing the characteristics by which they are judged.

W. C. Spackman

LABOUR

14. **The Feedback Principle in Elective Induction of Labor with Oxytocin Drip: A New Method.**

By C. S. Rights. *Obstet. and Gynec.*, **16**, 167–171, Aug. 1960. 4 figs. 27 refs.

Instead of the usual slow, continuous, intravenous administration of oxytocin for induction of labour, the author has devised a method whereby the control of the drip can be done on the feedback principle. The drip is controlled by a method in which uterine contractions shut off the inflow of oxytocin, and relaxation of the uterus permits it to flow again. The tubing from the oxytocin solution bottle is led under a belt fixed to the abdomen between the opposing edges of a plastic container and then to the intravenous site. The mechanism is adjusted so that a uterine contraction at its height stops the infusion.

This method is relatively simple, but the principle could be elaborated, perhaps using electrical or chemo-electric energy in the feedback.

J. G. Dumoulin

15. **The Value and Danger of Exogenous Oxytocin in Obstetrics.**

By C. L. Buxton and R. Hausknecht. *Amer. J. Obstet. Gynec.*, **80**, 32–37, July 1960. 3 tables. 12 refs.

During the two years 1957–58 oxytocin was used for induction of labour in 541 out of 9,908 patients, public and private, at Grace Newhaven Hospital. A solution of 1 ml. (10 units) per 1,000 ml. of 5 per cent glucose was commonly used, starting at 8 drops per minute. If necessary 4 or 5 attempts at induction with oxytocin are made on successive days before resort to Caesarean section.

No elective induction should be carried out unless the cervix is "negotiable" and the foetal head engaged. The patient should be fully aware of the reason for induction and it should not be done if she or her husband has any doubts whatever concerning its advisability. There were no maternal deaths and the corrected foetal mortality was 2·04 per cent. The Caesarean section rate is not given. There was no apparent increase in obstetrical complications. High tribute is paid to G. W. Theobald for introducing the intravenous drip which the authors consider perfectly safe if appropriate precautions are taken and safeguards strictly adhered to.

F. J. Browne

16. **The Electronic Evaluation of Fetal Heart Rate. III. The Effect of an Oxytocic Agent Used for the Induction of Labor.**

By O. W. Hess and E. H. Hon. *Amer. J. Obstet. Gynec.*, **80**, 558–567, Sept. 1960. 9 figs. 33 refs.

This is a study of the effect of oxytocin induction of labour on the pattern of the foetal heart rate. The oxytocin was administered by intravenous drip, 10 units of oxytocin being added to 1,000 ml. of 5 per cent dextrose in water, and the flow regulated until uterine contractions ensued. Membranes were left intact but in certain patients transabdominal amnioncentesis was done, followed by introduction of a small polyethylene tube to permit determination of amniotic fluid pressure. The foetal heart rate was recorded with the electronic techniques previously described by the authors.

The effect of the uterine contractions on foetal heart rates seemed to be determined largely by the frequency, duration and intensity of contractions. When they occurred at a rate of 4 every 10 minutes and lasted 40 to 60 seconds the rate was unchanged. In such cases the amniotic fluid pressure showed a peak intensity of 60 to 70 mm. Hg with 8 to 10 mm. Hg tonus between contractions. In some patients even though contractions were strong and very frequent there was little effect on foetal heart rate, which may denote an above average competency of the maternal-foetal vascular system.

One patient who was very sensitive had almost immediately after starting the drip a tetanic uterine contraction with uterine tonus raised to 20 mm. Hg. There was mild tachycardia and irregularity, followed by marked bradycardia and irregularity, and this in turn by tachycardia and irregularity.

Cases are cited illustrating variations in foetal reserve. One such was pre-eclampsia with blood pressure 190/130. Though the contractions following oxytocin induction were mild and of short duration bradycardia became profound, and Caesarean section was done. The baby weighed 3,175 grams and was in poor condition and the liquor amnii was heavily stained with meconium. Another patient at 43 weeks gestation had pre-eclampsia and a blood pressure of 160/95. Contractions were mild, but mild irregularity and tachycardia occurred followed

by sustained bradycardia. Caesarean section was done, and the 3,200 gram infant was cyanotic and limp and the amniotic fluid heavily meconium stained. The bradycardia is probably hypoxic in origin and was occasionally preceded and followed by mild tachycardia.

Previous studies of the haemodynamics of uterine contraction showed that the maternal blood flow through the intervillous spaces is impeded and may be cut off entirely at the height of the contraction, and if uterine hypertonus is present this space may be physiologically isolated and foetal oxygen reserves depleted. It would seem therefore that while oxytocin is an excellent method of inducing labour its use should be carefully supervised, as it may interfere with foetal oxygenation, especially if foetal circulatory reserve is compromised by maternal age, pre-eclampsia, maternal hypotension and perhaps postmaturity. *F. J. Browne*

17. **Stimulation of Uterine Contractions by Deep Breathing.**

By V. D. Petrescu and M. Demetrescu. *Obstet. si Ginec.*, pp. 31–34, Jan. 1960. 1 fig. 4 refs.

In the course of the research on uterine activity the authors have noticed a connexion between deep breathing and the uterine excitability. There is an increase in the excitability and activity of the myometrium after deep breathing. They have used an electroencephalogram apparatus and amplifier which records the activity of the myometrium.

In some control cases they have used oxytocic drugs, which gave the same pattern of uterine contractions as those produced by deep breathing. They have used 25 patients for this research, whose pregnancies varied from 4 months to full term. The electrohistogram showed that after 1–2 seconds of deep breathing there was electric activity in the myometrium which lasted 4–6 seconds.

The practical point is that deep breathing stimulates the action of the uterus during labour. The use of deep breathing in psycho-analgesia is important for both the improvement and shortening of labour. *Sylvia Lerer*

18. **Hypnosis in Obstetrics and Gynecology.**

By K. S. Tom. *Obstet. and Gynec.*, **16**, 222–226, Aug. 1960. 3 tables. 7 refs.

Success in induction of hypnosis is dependent on the method of induction, the prestige and experience of the operator, and the susceptibility of the subject. The technique may be visual, auditory or tactile stimulation, a combination of methods probably being the most effective.

To evaluate the effectiveness of hypnosis in labour, it was used by the author in 73 unselected volunteers. Preparatory sessions were started in the seventh month of pregnancy. The results showed that the method worked best in multiparous patients but was successful in only 40 per cent of cases, so that the author concludes that hypnosis is time-consuming and only has a very limited place in obstetrics. *J. G. Dumoulin*

LACTATION

19. **Fluorine in Human Milk.**

By B. Bercovici, I. Gedalia and A. Brzezinski. *Obstet. and Gynec.*, **16**, 319–321, Sept. 1960. 3 tables. 13 refs.

From Jerusalem comes this report on the amount of fluorine in human milk and urine samples from 62 lactating women and urine samples from 15 non-lactating women after delivery. All drank from the same water supply. The mean fluorine value in the milk was low and constant, whereas the value in the urine, originally low, increased gradually to reach the normal urinary fluorine value of adult males and non-pregnant women about 4 months after delivery. The maternal fluorine reserves appear to be depleted by pregnancy.

J. G. Dumoulin

INFANT

20. **The Effect of Maternal Factors upon the Mechanism of Fetal Oxygenation in the Normal Obstetric Patient.**

By J. A. Low. *Obstet. and Gynec.*, **16**, 146–151, Aug. 1960. 5 tables. 3 figs. 6 refs.

In a previous report the author studied the oxygen capacity in the umbilical vein and artery of 750 normal cases. The figures have been further analyzed and they show that maternal age does not affect foetal oxygenation. Primiparae have a higher oxygen capacity, lower umbilical vein content and saturation, and smaller tissue oxygen uptake. This is probably due to a variation in the pattern but not efficiency of placental function. The postmature pregnancy has a lower umbilical artery oxygen content and saturation with a higher coefficient of oxygen utilization, which may be an expression of reduced oxygen reserve if not oxygen want. *J. G. Dumoulin*

21. **An Electric Neonatal Respiratory Monitor.**

By W. E. B. Edge and W. E. Eaton. *S. Afr. med. J.*, **34**, 780–781, Sept. 10, 1960. 1 fig. 2 refs.

The author describes an apparatus which he has used with success for the early detection of apnoeic attacks. Thus babies liable to cyanotic episodes will not have to be "specialled" for the first week and the nursing staff will be notified by an extension alarm when apnoea has lasted for 15 seconds. The apparatus consists of (*a*) a respiratory motion detector or transducer, (*b*) a respiratory-pulse integrator and alarm control and (*c*) an extension alarm. The transducer consists of a length of rubber tubing packed with carbon granules which is strapped over the baby's upper abdomen. The varying electronic pulse developed with the aid of the detector is amplified and caused to pass to an integrating circuit, the output of which is a function of respiratory amplitude and periodicity. This pulse is used to charge a reservoir capacitor and an electromechanical switch is held in the "off" position as long as the integrated output exceeds a certain level. Should respiratory motion cease, the capacitor slowly discharges, and at the critical level the relay reverts to the "on" position, thereby completing an alarm circuit. *L. J. Abramowitz*

22. **Foetal Blood Loss by Way of the Maternal Circulation: A Cause of Anaemia in the Newborn.** (Feto-maternale Blutung als Ursache von Neugeborenen-anämie.)

By K. H. MANNHERZ. *Zbl. Gynäk.*, **82,** 1252–1257. Aug. 13, 1960. 2 figs. 24 refs.

The author reports that after a low forceps delivery for foetal distress the child cried readily but looked very pale. The clinical impression of anaemia was confirmed by a blood count showing a haemoglobin value of 54 per cent with 2,500,000 red cells. Haemolytic anaemia was considered at first but the Coombs test proved to be negative and the blood of both mother and child was Rhesus positive, group O. Later search failed to disclose any other type of antibody.

Examination of the maternal blood, however, revealed 7·3 per cent foetal haemoglobin. This suggests that the foetal bleeding into the maternal circulation must have amounted to about 250 ml., though it may have occurred over a prolonged period of time.

Bruce Eton

23. **Surgery in the Newborn.**

By J. H. LOUW. *S. Afr. med. J.*, **34,** 686–695, Aug. 13; 707–713, Aug. 20, 1960. 5 tables. 17 figs. 66 refs.

The author deals with all facets of neonatal surgery. In 9 years 406 cases have been treated in his unit, an incidence of 2·5 "surgical cases" per 1,000 live births. Uncontrollable factors which adversely affected results were multiple congenital abnormalities (which occurred in 25 per cent of cases) and prematurity (in 50 per cent of cases). There are very many controllable factors. Scrupulous attention to detail is the secret of success. Delay in diagnosis results in a rise in mortality from 20 per cent on the first day to 83 per cent on the sixth day. The recognition of prenatal warning signs, thorough examination of the infant at birth, awareness of significance of cyanosis, vomiting and drooling, and the uses and abuses of radiological examination are fully discussed. Concentration of these patients in a central paediatric surgical unit is essential, and the author deals with transport facilities to the centre, the locality of the centre and personnel. Special features of the pre-operative management are minimal interference, constant observation, isolation, control of the environment, prevention of suffocation, gastro-intestinal decompression and hydration. The value of blood transfusion, antibiotics and vitamins is also discussed. The timing of the operation, anaesthesia, the control of body temperature, blood volume, tracheo-bronchial toilet and surgical technique are all considered. Post-operative care is given detailed attention.

L. J. Abramowitz

24. **Microsomia Fetalis.**

By C. T. JAVERT. *Amer. J. Obstet. Gynec.*, **80,** 579–581, Sept. 1960. 7 refs.

The microsomic infant, because it weighs less than 2,500 grams at birth is classed as premature. The author had 9 cases in 700 private obstetric patients (1·3 per cent). All pregnancies were apparently normal. The condition was associated with a small fibrous looking placenta (under 600 grammes) and often with a thin umbilical cord with spiralled vessels and little jelly of Wharton. At birth the infant, besides being small, has a stunted appearance with a wrinkled dry skin without much subcutaneous fat. The nails are long. Except for difference in size and weight it resembles the so-called postmature baby of Clifford and the dysmature infant of Sjostedt and associates. All the author's babies were born alive, took to the bottle with gusto and started to gain weight almost at once. Thereafter growth and development were rapid.

F. J. Browne

25. **The Aetiology of Congenital Malformation.** (Zur Frage der Ätiologie der Missbildungen.)

By I. KOVÁCS and L. MAKAY. *Zbl. Gynäk.*, **82,** 1335–1341, Aug. 27, 1960. 5 tables. 2 figs. 17 refs.

The authors briefly review 158 cases of congenital malformations occurring amongst 12,232 children born during the 20 years 1938–1957, an incidence of 1·2 per cent. A diagram showing the annual incidence reveals marked peaks about 1946 and 1953, reaching 2 per cent. The first peak is attributed to the poor economic and social conditions after the war and the second to a severe epidemic of influenza.

More than half the malformations were of the neuro-ectodermal type. The incidence of foetal malformations rose with the age of the mother. An attempt to draw conclusions from the maternal history regarding the aetiology of congenital malformations, suggested that the environmental conditions of the expectant mother may have considerable influence on intra-uterine development of the foetus.

Hitherto the emphasis of antenatal care was on the prevention of toxaemia and of mechanical complications. The author recommends that more attention should be paid to the avoidance of factors which may predispose to congenital malformations.

Bruce Eton

26. **Foetal Malformations During the Period of a Pandemic of Influenza with the Virus "Singapore A".** (Malconformazioni fetali nel periodo della pandemia influenzale da virus "Singapore A".)

By V. PICCIONI and S. BETTOCCHI. *Ann. Ostet. Ginec.*, **82,** 842, July 1960. 40 refs.

During September to December, 1957 there was an epidemic of influenza caused by the Singapore virus A in the Rome area. An analysis has been made of congenital defects in newborn infants born in the first eight months of 1958.

There was, compared with preceding years, a definite increase in the incidence of congenital anomalies. The figure in 1958 was 0·95 per cent, as against 0·42 per cent in 1957 and 0·59 per cent in 1956.

It is concluded that a small number of the congenital anomalies described in 1958 can be ascribed to the influenza virus, though the possible effects of drugs given to treat influenza cannot be excluded.

Josephine Barnes

27. **Can the Perinatal Mortality be Reduced by Active Management of Labour?** (Kann die perinatale Kindersterblichkeit durch aktivere Geburtsleitung verbessert werden?)

By H. TASCH. *Zbl. Gynäk.*, **82**, 1276-1283, Aug. 13, 1960. 8 tables.

The author compares the perinatal mortality of two successive 4-year periods between 1952 and 1959. Of a total of 13,420 births, 394 children (2·8 per cent), weighing at least 1,000 g. were either stillborn or died within the first 10 days of life. The cause of death was more often unknown in the earlier group.

During the first 4 years the practice of midwifery was strictly conservative. Confinements were primarily in the hands of midwives. Medical aid was sought when complications had developed. Oxytocic drugs before delivery were avoided and the indications for forceps and Caesarean section were comparatively restricted. The perinatal mortality was 3·4 per cent. Of these children 54·2 per cent died during operative vaginal delivery. The incidence of birth trauma was 11·1 per cent during spontaneous births. Episiotomy was carried out in 15·2 per cent of cases, the forceps rate was 1·1 per cent and the Caesarean section rate 2·1 per cent.

The head of the department changed in 1956. A more active policy of management of labour was adopted. The idea that the child was safe as long as the membranes were intact was dismissed. A careful assessment of uterine function was made in the early stages of labour and, in the light of modern knowledge of uterine physiology, oxytocic drugs were used in selected cases during labour. Episiotomy, forceps and Caesarean section were employed more liberally and during the subsequent 4 years the incidence of the 3 operations increased respectively to 26·1 per cent, 4 per cent and 3·2 per cent, whereas the perinatal mortality dropped to 2·5 per cent. The use of episiotomy was extended particularly in the case of premature babies.

The maternal mortality during the two periods changed from 0·06 to 0·05 per cent.

44·2 per cent of the children lost during the second period died during operative vaginal delivery.

[This figure may be partly due to the more liberal use of forceps, so that cases with relatively little risk diluted the forceps group. A favourable conclusion can only be drawn from the overall perinatal mortality which was reduced from 3·4 to 2·5 per cent.] *Bruce Eton*

GYNAECOLOGY

28. **Growth Characteristics of Human Endometrium in Tissue Culture.**

By D. C. FIGGE. *Obstet. and Gynec.*, **16**, 269–277, Sept. 1960. 7 figs. 9 refs.

When growth of human endometrium occurs in tissue culture it is generally evident within 72 hours, although a delay as long as 7 days has been noticed. Cells from the proliferative phase of the menstrual cycle grow best. Two distinct patterns of growth are noted: reticular growth and epithelial growth. Reticular or fibroblastic growth is a loose meshwork of spindle-cells attached by slender tapering processes. In epithelial growth polygonal cells are seen often in sheets.

Many believe that the stromal cell proliferates as a reticular outgrowth and the gland cell in epithelial sheets, but there is some doubt about this, and the author believes that both may represent glandular growth under different influences.

The variation in glycogen and nuclear protein concentrations observed during the changing phase of *in vivo* endometrium does not occur in tissue culture growths derived from this parent endometrium. The endometrium in culture fails to maintain the physiological potentials of the antecedent tissue. *J. G. Dumoulin*

29. **Pancreatic Enzymes (Cervase) in Gynecology.**

By J. I. BISKIND and L. H. BISKIND. *Obstet. and Gynec.*, **16**, 202–205, Aug. 1960. 4 refs.

Cervase, made up in tablet form, is derived from desiccated pancreas and contains trypsin and amylase. It causes debridement of dead or necrotic tissue and seemed to be a fairly effective way of treating cervicitis, post-operative granulation tissue, chemical burns of the vagina and non-specific leucorrhoea. *J. G. Dumoulin*

30. **Congenital Adrenal Hyperplasia Producing Female Hermaphroditism with Phallic Urethra.**

By L. A. PERIS. *Obstet. and Gynec.*, **16**, 156–166, Aug. 1960. 2 figs. 45 refs.

A case of female hermaphroditism with phallic urethra due to congenital adrenal hyperplasia is reported. The patient, an 18-year-old male, had 3 episodes of haematuria thought to be due to menstruation. The penis was very small. The scrotum was empty and both inguinal canals had been explored at the age of 12 for testes, but none were found. Sex chromatin examination showed the female pattern. Urethroscopy revealed a vagina and cervix. Psychological evaluation revealed masculine interests. Abdominal total hysterectomy with removal of ovaries was performed and vitallium spheres were inserted into the empty scrotum. Testosterone treatment was given.

A review of the literature reveals that this is the eleventh such case. The aetiology of the condition is reviewed together with the embryology of sexual differentiation. Diagnosis and treatment are discussed. The author considers that if a diagnosis is made before the age of 2, the child should be made a female and given cortisone therapy for life. If the child is more than 2 years old and less than 7 or 8, he should be treated as a male and given cortisone to permit further bone growth, unless by then epiphyseal closure has already occurred: cortisone should not be given if the bone age is over 12 years as it will cause feminization unless the ovaries are removed. If the child is treated as a male, ovaries and uterus should be removed, and testosterone is used to develop the phallus.

The psychiatric and medicolegal aspects of the subject are also discussed. *J. G. Dumoulin*

31. **Preliminary Observations on 218 Women Who Have Received Orthogenetic Advice. The Technique and Mental Prophylaxis.** (Observations préliminaires sur 218 femmes ayant reçu des conseils medicaux d'orthogénisme: technique et prophylaxie mentale.)

By LAGROUA-WEILL-HALLÉ. *Gynéc. prat.*, **11**, 309–352, 1960.

This long article is a well-documented plea for contraception in a country where it meets with stern official disapproval.

The author prefers to replace the term "Birth Control" by "Orthogenetics", as she feels that the medical attitude towards this problem should be one of the organization of conceptions so that they occur under the best possible physical, moral, economic and social circumstances of each individual family.

[In this question the British obstetrician is better placed than his French colleague and will have little to learn from this article. None-the-less it merits attention as an obviously sincere attempt to gain recognition of contraception as a method of improving maternal health and reducing the number of illegal abortions.]

Geoffrey Dixon

32. **Reflux of Blood into the Uterine Tubes as a Possible Cause of Sterility Following Abortion.** (Rückfluss des Blutes in die Eileiter als mögliche Ursache der Sterilität nach Fehlgeburt.)

By H. DYKOVÁ, F. HAVRÁNEK and J. POSPÍŠIL. *Zbl. Gynäk.*, **82**, 1228–1236, Aug. 6, 1960. 8 figs. 16 refs.

Although the majority of cases of secondary infertility is due to tubal blockage, clinical manifestations suggesting an infective process are commonly absent. This fact led the authors to investigate the histological condition of the tubes following abortion. The clinical material consisted of 11 women who were sterilized by salpingectomy after termination of pregnancy. The tubes were removed immediately or within a few hours of abortion in 5 women and after 3, 4, 6, 7 and 9 days in the others. The excision was performed with special care in order to avoid traumatic artefacts. The tubes of 10 non-pregnant women subjected to hysterectomy who were not bleeding at the time of the operation served as controls.

Massive haemorrhage or blood clots were found in six abortion cases but in none of the controls.

The authors believe that an intra-tubal haematoma or clot may become organized, or that the blood may serve as a pabulum for ascending bacteria, causing an inflammatory process which, in some cases, may lead to tubal occlusion.

Bruce Eton

33. **The Efficacy of a Modern Treatment of Male Subfertility.** (D'un traitement moderne de la subfertilité masculine.)

By C. BALLERIO and A. GIAROLA. *Gynéc. prat.*, **11**, 143–147, 1960.

After a brief consideration of the therapeutic agents available for the improvement of male subfertility, the authors give their reasons for their selection of the amino acid arginine.

They have given 8 to 12 g. of this substance daily for periods of 40 to 60 days to 20 men, all of whom had seminal specimens below the accepted criteria of 1·5 ml. volume, 30 millions per ml. count with a 70 per cent motility after one hour and 30 per cent after 9 hours.

The average count of 19·5 million per ml. was improved to 39·8 millions after treatment. Improvement in volume and motility also resulted. Eight pregnancies have occurred in this series; one ended in a three months' abortion.

[Not the least interesting part of this article is the authors' footnote explaining its previous non-appearance in print.]

Geoffrey Dixon

INFECTIONS OF THE REPRODUCTIVE ORGANS

34. **Treatment of Vaginitis with Triclobisonium Chloride.**

By J. P. DEMETRY and R. R. HANSEN. *Obstet. and Gynec.*, **16**, 189–193, Aug. 1960. 3 tables. 3 figs. 18 refs.

Hoping to find a therapeutic agent useful for all types of vaginitis, the authors tried 0·1 per cent triclobisonium chloride in a cream base in 84 cases. The overall success rate was 92 per cent. The agent seemed to have a high antibacterial and antitrichomonal activity, together with a moderate antifungal activity.

J. G. Dumoulin

35. **Female Genital Tuberculosis in Children and Adolescents.** (La tuberculose génitale chez les fillettes et les adolescentes.)

By K. VACHA. *Gynéc. prat.*, **11**, 297–302, 1960.

Of 127 cases of genital tuberculosis 35·4 per cent were thought to have arisen at or near the time of the menarche. In 8 young girls the diagnosis was made at the time of their first period; in 8 more during their first year of menstrual life and in 29 before marriage.

Genital tuberculosis must be suspected in any girl afflicted with a primary tuberculous lesion at or near the time of the menarche, and all such patients should be seen and followed up by a gynaecologist. Menstrual culture and guinea-pig inoculation should be carried out and endometrial biopsy is not to be avoided in such patients.

The results of treatment are improved by early diagnosis.

[Unfortunately, beyond saying that "we ourselves possess 5 cases of term pregnancy after anti-tuberculous therapy" the author gives no details of his results.

Frequent undated references to other authors occur in the text but no table of references is given. The article has been translated from its original Czechoslovakian into French.]

Geoffrey Dixon

36. **Frequency and Treatment of Vulvo-Vaginal Mycoses in the Non-Pregnant.** (Quelques remarques sur la fréquence et le traitement des mycoses vulvo-vaginales non gravidiques.)

By J. P. PUNDEL, E. OST and P. MOITZHEIM. *Gynéc. prat.*, **11**, 285–296, 1960.

The frequency of mycotic infections of the vulva and vagina is increasing. It is suggested that this increase is due to the liberal and often unwise use of the broad spectrum antibiotics. The evidence brought forward to support this claim is that of 109 women with candida infections 22 per cent had noticed the onset of symptoms during or immediately after finishing a course of antibiotics. In 39 per cent there was a history of antibiotic therapy between 2 and 12 months previously. Many other women had received injections or tablets, the nature of which was unknown to them. In only 20 per cent of the cases could previous antibiotic therapy be excluded.

The diagnosis must be supported by the clinical findings, direct microscopy of the discharge and culture. The authors prefer Loeffler's medium to that of Nickeson which they feel may give rise to falsely positive culture results.

The classical methods of treatment were disappointing and gave only 15 per cent of cures in 200 women. Mycostatin applied vaginally together with a simple antiseptic lotion for the vulva gave a 99 per cent cure rate in 250 women.

There was a 2 per cent relapse rate. Three of these 5 patients were found to harbour candida in the tonsils and some form of candida infection was found in the husbands of the two others. Treatment of these secondary foci of infection produced permanent cure when combined with a second vaginal treatment. The authors consider that Mycostatin should be the treatment of choice in vulvo-vaginal mycoses. *Geoffrey Dixon*

37. **Some Characteristics of Vaginal Smears in Trichomoniasis.** (Niektore cechy rozmazu pochwowego w rzesistkowicy.)

By E. GRYS. *Ginek. pol.*, **31**, 321–332. 1960. 2 tables. 6 figs. 18 refs.

The author describes a characteristic conglomeration of leucocytes in rosette form which indicates trichomonal infection in the vaginal smear.

He examined 971 patients who were referred for a cytological opinion. In 316 (32·5 per cent) trichomonas was present. In 216 (22·2 per cent) out of the total number the characteristic leucocyte "rosettes" were present. Out of 216 women with "leucocyte rosettes" in vaginal smears trichomonas vaginalis was found in 202 (93·5 per cent).

"Leucocyte rosettes" in the vaginal smear are easily detected and prove the presence of a trichomonal infection. *S. H. Riterband*

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

38. **Pelvic Perfusion with Nitrogen Mustard for Cancer: A Neurological Complication.**

By D. M. SHOLES. *Amer. J. Obstet. Gynec.*, **80**, 481–484, Sept. 1960. 1 fig. 18 refs.

The use of nitrogen mustard by the perfusion technique is known to cause generalized bone marrow depression when circulatory isolation is incomplete, and recent work also suggests that it is strongly neurotoxic. The author reports the case of a patient aged 47 years who sustained peripheral nerve damage following perfusion with HN_2 for a metastatic endometrial cancer with spread confined to the pelvis. Three weeks after panhysterectomy and after isolation of the pelvic circulation the patient was subjected to pelvic intra-arterial perfusion of 60 mg. of HN_2 in isotonic saline in 4 equally divided doses at 15 minute intervals. Apart from temporary haemopoietic depression and skin pustules over sacrum, perineum and upper thigh, recovery was uneventful, but two months after discharge from hospital she returned because of pain, right foot drop, and paralysis of the hamstrings and muscles below the right knee. It was eventually concluded that damage had occurred to the lumbo-sacral plexus but whether this was due to the toxicity of the nitrogen mustard or to damage of the local blood supply was not determined. Now, two years after operation the patient is able to walk with crutches and there is no evidence of recurrence of malignancy. Experimental data suggest that neuro-toxicity rather than damage to the bone marrow may be the chief limiting factor in the use of high dosages of nitrogen mustard in perfusion techniques. *F. J. Browne*

39. **Mesonephric Carcinoma of Cervix Uteri.**

By H. C. STEARNS and V. D. SNEEDEN. *West. J. Surg., Obstet. Gynec.*, **68**, 249–255, July–Aug. 1960. 10 figs. 9 refs.

The remnants of the mesonephric ducts penetrate the cervix to varying depths and a cancer arising in them is hidden until it is very advanced; this might account for many well-advanced growths in patients whose signs and symptoms are of recent origin. Two types of tumour are recognized, one being adenomatous and resembling the granulosa-cell tumour while the other is a spindle cell tumour resembling embryonic connective tissue. Early lesions are classically lateral and present on the portio, upper vagina or within the endocervical canal. The pathologist may obtain help by using mucicarmine stains to differentiate persisting mesonephric ducts and tubules from deeply buried endocervical glands. Four cases are described and the author thinks that the lesion is perhaps not uncommon. *D. C. A. Bevis*

40. **The Results of Treatment of Carcinoma of the Cervix Associated with Pregnancy.** (Behandlung und Ergebnisse beim Kollumkarzinom in der Schwangerschaft.)

By G. SCHUBERT. *Geburtsh. u. Frauenheilk.*, **20**, 1124–1128, Oct. 1960. 1 table. 25 refs.

Twelve cases of carcinoma of the cervix associated with pregnancy were treated from 1950–1954 in the University Gynaecological Clinic, Hamburg-Eppendorf. In 7 cases the patients were symptom-free and the lesion was discovered on routine speculum, colposcopic and

cytological examination. In 8 cases carcinoma of the cervix was diagnosed in the first 20 weeks of pregnancy. In 7 the growth was stage I, in 3 stage II and in 2 stage III.

Two early cases were treated by Wertheim's hysterectomy followed by irradiation. In the 6 other cases diagnosed during early pregnancy treatment was begun by insertion of radium into the uterus and vagina; in 5 of these cases treatment was completed by sub-total hysterectomy and bilateral salpingo-oöphorectomy followed by further irradiation with radium and X-rays. In the remaining case insertion of radium was followed by spontaneous abortion and treatment was then completed by curettage and further radium insertions and X-irradiation.

The 4 cases diagnosed after the 20th week of pregnancy were delivered by Caesarean section, which was followed by sub-total hysterectomy and bilateral salpingo-oöphorectomy (Porro's operation); treatment was completed by insertion of radium, beginning 10 days after operation, and by X-ray therapy. Two of these infants survived. The author does not believe that postponement of treatment until the 36th week in order to obtain a more mature infant can be justified.

One patient with a stage III carcinoma of the cervix diagnosed in the 3rd month of pregnancy and treated by radium, sub-total hysterectomy, etc., died the year after the diagnosis had been made. All the other patients are alive and with no sign of recurrence 5 years or more after treatment began.

Peter J. Huntingford

41. **Pregnancy, An Opportunity for the Detection of Early Cancer.** (Die Schwangerschaft als Engpass in der Krebsfährtensuche.)

By J. JENNY, H. J. WYSS, A. WACECK, J. H. MÜLLER and E. HELD. *Geburtsh. u. Frauenheilk.*, **20**, 1136–1152, Oct. 1960. 8 tables. 8 refs.

In the University Gynaecological Clinic, Zürich, 458 women, who were admitted for termination of pregnancy, were subjected to routine colposcopic, cytological and histological examination of the cervix; in addition 32 women were similarly investigated during the later weeks of pregnancy. Wedge biopsies were taken from the anterior and posterior lips of the cervix. It was found that pregnancy did not influence the colposcopic picture and the correlation between colposcopy and the histological findings was unaffected. The evaluation of vaginal smears was rendered a little more difficult because of increased desquamation, the presence of inflammatory cells and an increase in nuclear size.

No case of invasive carcinoma was found. In 6 cases histological examination showed the changes of carcinoma *in situ* and in 4 of them these changes persisted after termination of the pregnancy. There were 4 other patients with abnormally active cervical epithelium and 7 with basal cell hyperplasia; on follow-up examination of these patients 1 from each group was later found to have pre-invasive carcinoma of the cervix. One patient had suspicious changes of the cervix on colposcopy although histologically the tissues were normal; 5 years later this patient developed carcinoma *in situ*. The relative values of colposcopy and cytology for the screening of pregnant patients are discussed. The authors believe that the search for early malignant changes of the cervical epithelium during pregnancy is justified.

Peter J. Huntingford

42. **Preinvasive Cervical Lesions in Obstetric Patients: Methods of Diagnosis, Course, and Clinical Management.**

By L. D. JOHNSON, A. T. HERTIG, C. H. HINMAN and C. L. EASTERDAY. *Obstet. and Gynec.*, **16**, 133–145, Aug. 1960. 4 tables. 8 figs. 13 refs.

This is a long report on a large series of cervical examinations done on pre- and post-partum patients over a 10-year period at Boston. The Schiller test was used extensively and was found to be positive in erosions with pre-invasive lesions. A new method of taking multiple punch biopsies, consisting of radial-step biopsies followed by circumferential ones is described which has the advantages of a diagnostic conization without its dangers.

Pregnancy and delivery did not appear to have any dramatic effect on cases of carcinoma *in situ*. In 119 cases of anaplasia, only 1 progressed to carcinoma, so that it would seem justifiable to remove the area of anaplasia by conization or cauterization so long as careful follow-up is possible. Areas of anaplasia frequently regressed within 18 months of their discovery, but recurred in 6 cases. In cases with pre-invasive lesions, normal delivery is allowed so long as there is no evidence of stromal invasion. After post-partum re-evaluation, these lesions are treated by simple hysterectomy or conization, depending on the particular case.

Post-partum cauterization of clinically abnormal cervices is inadequate as a means of treating pre-invasive lesions or preventing cancer.

J. G. Dumoulin

43. **Surgical Management of Carcinoma of the Cervix.**

By J. W. KELSO. *West. J. Surg., Obstet. Gynec.*, **68**, 201–207, July–Aug. 1960. 9 tables. 6 refs.

The Professor of Gynaecology in the University of Oklahoma presents the results of surgery in 120 patients followed for over 5 years from operation. Cases were unselected and ranged in age from 22 to 76. A radical Wertheim hysterectomy taking the upper third or half of the vagina was performed, followed in some cases by deep X-ray therapy. Of 71 cases in Stage 1 62 have survived (87 per cent); 49 cases in Stage 2, 36 have survived (73 per cent). In 21 patients nodal metastasis was demonstrated and 11 have survived. Five patients were pregnant and all are alive and well; 7 patients had stump carcinoma and all these are alive and well. Seven patients died immediately after operation and 16 developed fistulae but the author points out that to be effective, operation must verge on the heroic and he is prepared to accept these risks. He stresses that early treatment is imperative and is therefore against radiosensitivity tests, etc.

[This is a very full review of the cases treated and the original paper must be consulted for full details.]

D. C. A. Bevis

44. A Study of Complications in the Surgical and Radiation Therapy of Cancer of the Cervix.

By H. C. Frick, H. C. Taylor, Jr., R. J. Guttmann, H. W. Jacox and W. P. McKelway. *Surg. Gynec. Obstet.*, **111**, 493–506, Oct. 1960. 14 tables. 2 figs. 27 refs.

The authors discuss the rise in frequency of injuries consequent on the increasing extent of surgical treatment and increasing dosage of radiotherapy in the treatment of carcinoma of the cervix, and point out that a time is reached when complications bar further extension of therapy. An attempt is made to compare the two forms of treatment, with respect to complications, and to define the limits of therapy, especially radiation dosage, at which the complication rate seems so great as to preclude further increase in therapy.

Seven hundred and forty-eight cases, occurring between 1944 and 1957, are reviewed, treatment being by external radiation in 82, intracavity radium and external radiation in 272, radium needles and external radiation in 119, intracavity radium, external radiation and lymph node dissection in 56, radical operation in 92 and radical operation plus external radiation in 115. Twelve cases were treated by other methods. The cases were divided into those occurring before and those occurring after 1952, as at this time supervoltage therapy became available and some patients were subjected to extraperitoneal node dissection after full radiation therapy.

Radiation injuries from supervoltage therapy included intestinal (early entero-colitis; later obstruction and perforation from endarteritis), urinary (cystitis, haematuria and fistula formation), osseous (spontaneous hip fracture due to endarteritis) and cutaneous (less common with supervoltage therapy). Increased dosage can be delivered with supervoltage therapy without the skin reaction limiting therapy and the authors quote reports on cases where injuries have increased as the tumour dosage exceeds 3,000 r. Some deaths are also directly attributable to radiation injury.

Surgical complications are mentioned, early ones being less commonly seen but the most important later one, uretero-vaginal fistula, apparently not decreasing in frequency.

Analyzing the complications in the various groups mentioned, it was noted that injuries were more common if 4,000 r. or more were given over 4–6 weeks to the lateral pelvic wall, and that injuries were more frequent in cases treated by extraperitoneal node dissection following radiation. The authors concluded that the latter form of therapy should be abandoned and that the external radiation should be reduced to 4,000 r. to the lateral pelvic walls (except in Stage 3 and 4 growths, where intracavity radium dosage may be reduced). Stricter selection of cases is recommended in order to reduce operative complications.

A. E. R. Buckle

45. The Pathology of the Cervical Stump. (La pathologie du col restant.)

By E. Moracci. *Gynéc. prat.*, **11**, 217–232, 1960. 53 refs.

This paper is an exhaustive review of both the literature on the subject and of 96 patients seen in 22 years with pathology of the cervical stump.

The lesions present were as follows:

Inflammatory disease	47 cases
Carcinoma	23 cases
Prolapse	9 cases
Pelvic pain	8 cases
Fibromyoma	4 cases
Polyp	4 cases
Sarcoma	1 case

In 61 of the 96 patients treatment involved excision of the stump.

For Stage I carcinoma of the stump the author has practised excision of the stump and parametrial tissue together with partial excision of the vagina. This procedure is performed either vaginally or abdominally. More advanced lesions were treated by radium or combined radium and deep X-ray. The immediate results are described as "satisfactory" but apart from the fact that two patients (Stage II and Stage IV) deteriorated rapidly after radium therapy, no details are given.

The author agrees that prolapse of the stump is more common than prolapse of the vault after total hysterectomy. Although he is willing to concede that subtotal hysterectomy still has a place in gynaecological surgery, he feels that the total operation is in every way preferable unless the woman be under 40 years of age with a perfectly healthy cervix.

[This is a well-written article but, for the most part, simply advocates what is standard British practice.]

Geoffrey Dixon

46. Mesonephric Clear Cell Carcinoma of the Ovary: A Clinical and Pathologic Study.

By T. M. Parker, M. B. Dockerty and J. M. Randall. *Amer. J. Obstet. Gynec.*, **80**, 417–425, Sept. 1960. 4 figs. 11 refs.

Among the many and varied histopathological patterns seen in primary cancer of the ovary is one showing a preponderance of columnar cells with water-clear cytoplasm arranged in a pattern resembling that in renal hypernephroma. As far as at present known it arises in pre-mesonephric mesoderm. The present report deals with 24 of these tumours found among 1,192 primary ovarian cancers. The patients' ages ranged from 37 to 68 years (average 53). Five had a history of multiple familial carcinoma, defined as the occurrence of 3 or more malignant tumours in the immediate family (grandparents, parents, siblings or children).

The clinical features were those common to all primary ovarian cancers. Treatment was usually by total hysterectomy with bilateral salpingo-oöphorectomy and post-operative Roentgen therapy. Follow-up studies of 21 patients showed that only 5 were alive and without recurrence 5 or more years after operation.

Of 23 tumours where gross pathology was known 14 were cystic and 9 solid. Grossly there were no features to distinguish them from other cystic or solid tumours of the ovary, but in 3 of the solid tumours minute cysts embedded in dense fibrous stroma were visible with a hand lens and resembled the parvilocular ovarian tumours described by Schiller. Microscopically the characteristic feature was sheets of clear cells of uniform size and shape in a delicate vascular connective tissue stroma, or lining a tubular or cystic space. In some sections the stroma resembled a primitive mesenchyme from which it was apparently possible to observe the genesis of clear cells. In general, tubular, alveolar, parvilocular and papillary patterns could be recognized in each tumour. In no case did the histological pattern resemble the mesonephroma of Schiller. By special stains it could be shown that the clarity of the clear cells was not due to contained fat. The authors conclude that these clear cell cancers are a homogeneous group distinct from Schiller's mesonephroma.

F. J. Browne

47. **Radio-gold in the Treatment of Malignant Ovarian Tumours: Technique and Dosage.** (Problemi di tecnica e dosimetria nella terapia complementare dei tumori maligni del' ovaio con Au^{198}.)

By A. BARBANTI and A. TETTI. *Minerva ginec., Torino*, **12**, 683–686, July 31, 1960. 2 tables. 21 refs.

Of the radio-isotopes in use in the treatment of malignant disease of the ovary, including peritoneal involvement with effusion, the most useful has been radio-gold by reason of its physical characteristics, its lymphatic chemotaxis and its short hemiperiod. In Turin it has been used in over 100 cases endoperitoneally and by parametrial and endometrial application, both pre- and post-operatively, and no contra-indications nor ill-effects have been encountered. Certain precautions are necessary for the protection of the operator and all others who might be exposed to the radiation. The special syringe is guarded by lead and brass, and for endometrial application a distensible plastic container is shaped to occupy the uterine cavity. Speed with exactness and avoidance of close contact are required of the operator. The patient is warded in isolation and the nursing staff are on a strict rota. Visitors are excluded for five days and no young persons admitted. Unused material, dressings, instruments, discharges, etc., must be kept in protected containers for five hemiperiods.

The rest of the article deals with the calculation of the dosage and strength to be used for injection into the peritoneal cavity, depending largely on the amount of the ascitic fluid present. Provided the above technique is followed, a dosage in excess of that employed in other centres has been found feasible.

W. C. Spackman

48. **Androgen Excretion in a Case of Testicular Tubular Adenoma of the Testicle.** (Aspetti del ricambio androgeno in un caso di "adenoma tubulare testicolare dell' ovaio".)

By A. BOMPIANI. *Ann. Ostet. Ginec.*, **82**, 782, July 1960. 26 figs. 92 refs.

A case is described of a 22-year-old woman who presented with amenorrhoea, hirsutes and slight gain of weight but no alteration in the voice or libido. There was definite hypertrichosis with slight enlargement of the clitoris. Retro-pneumoperitoneum revealed no adrenal enlargement. Both ovaries were enlarged and at laparotomy, solid masses were excised from both ovaries. Histological examination of these revealed the histological structure of the testicular tubular adenoma of Pick (*Arch. Gynäk.*, 1905, **76**, 191). Excretion of androgen in the form of 17-keto-steroids fell immediately after removal of the tumours. Normal menstruation returned and nine months after the laparotomy the patient became pregnant.

Josephine Barnes

49. **Experimental Production of Endometrial Carcinoma in the Rabbit.**

By J. C. MERRIAM, C. L. EASTERDAY, D. G. MCKAY and A. T. HERTIG. *Obstet. and Gynec.*, **16**, 253–262, Sept. 1960. 14 figs. 9 refs.

Carcinoma of the endometrium was induced in rabbits by inserting into the uterus a string soaked in methylcholanthrene. Biopsies were taken every 2–3 months after insertion and the rabbits were killed after a year. The biopsies showed that there were progressive histological changes from hyperplasia of the endometrium, through carcinoma *in situ*, to invasive carcinoma. It is interesting that cystic hyperplasia is induced by a non-specific stimulus and usually precedes carcinoma.

The results of histochemical study of the rabbit endometrial carcinoma are also given and compared with studies on human tumours. Whilst many of the changes are similar, there are some inconsistencies which may be due to the non-cyclical nature of the rabbit endometrium or to the artificial method of induction of the rabbit tumours.

J. G. Dumoulin

50. **Significant Post-Menopausal Endometriosis.**

By R. D. KEMPERS, M. B. DOCKERTY, A. B. HUNT and R. E. SYMMONDS. *Surg. Gynec. Obstet.*, **111**, 348–357, Sept. 1960. 2 tables. 4 figs. 13 refs.

Endometriosis is seldom diagnosed clinically in the post-menopausal woman, it being believed that the endometriotic process undergoes atrophy and that the clinical features fade with the advent of the menopause.

Various authors have reported on symptom-producing cases of post-menopausal endometriosis, both external and internal, the "activity" being thought to result from persistence of a significant level of oestrogen after the menopause.

In a survey of 136 cases of post-menopausal external endometriosis reviewed by the authors, 41 were deemed to have clinically significant lesions, namely the presence of substantial intestinal endometriosis, widespread pelvic endometriosis and ovarian endometrial or tarry cysts greater than 3 cm. in diameter. Of these cases judged to be of clinical significance, in only 24 was the diagnosis proved histologically.

In a further group of 22 patients with post-menopausal

internal endometriosis, 2 cases were judged clinically significant.

The sites involved, in decreasing order of frequency, were the ovary, diffuse peritoneal involvement, intestine and vagina. Over 50 per cent of the patients with proven disease had undergone previous pelvic surgery.

Clinically, three groups were noted: (1) those with symptoms, (2) those without symptoms but with lesions requiring surgical exploration and (3) those without symptoms where endometriosis was found during the course of surgery for other conditions.

The macroscopic appearances of the lesions corresponded to those found in the younger age groups. Microscopically the endometriosis was of atrophic type in 21 of the histologically proven cases, the remainder showing varying degrees of activity, though in none was progestational epithelium encountered.

The authors emphasize that total hysterectomy and bilateral salpingo-oöphorectomy is a satisfactory method of treatment and that conservative management of involved intestine is usually possible.

A. E. R. Buckle

OPERATIONS

51. The Preventive Treatment of Thrombosis and Embolus in Abdominal and Gynaecological Surgery. (Sur le traitement préventif de la thrombo-embolie en chirurgie abdominale et gynécologique.)

By A. CHALLIER. *Gynéc. prat.*, **11**, 149–153, 1960.

The great variety of methods used in the prevention and treatment of post-operative venous thrombosis and embolism has prompted the author to describe once again the methods he has used with success for many years. Such thromboses are due to the interplay of two factors, blood stasis and blood hypercoagulability.

The first should be overcome by the pre-operative application of an adhesive elastic bandage from sole to thigh on each side, and by very early post-operative exercises and ambulation.

A simple test of clotting time should be carried out pre-operatively and on several occasions post-operatively. If the clotting time is ever less than 6 minutes the systemic use of oral anticoagulants in the first 10–12 post-operative days is advocated. The advent of calf tenderness is an indication for an immediate increase in the dosage of anticoagulant.

The only patient in the author's experience during the past 10 years who sustained a serious thrombosis was one who refused both early ambulation and the routine estimations of clotting time.

Geoffrey Dixon

52. Compound G-27202 in the Treatment of Thrombophlebitis.

By D. PENT and J. ROJAS. *Obstet. and Gynec.*, **16**, 206–209, Aug. 1960. 4 tables. 2 refs.

Previous experiments have shown that phenylbutazone (Butazolidin) is useful in treating superficial thrombophlebitis. A metabolic-excretion product of Butazolidin, compound G-27202, was used by the authors in 60 cases of superficial thrombophlebitis and 6 of deep thrombophlebitis. Patients received 200 mg. three times a day for 2 days, followed by 100 mg. three times a day.

Prompt improvement occurred in the first 24–48 hours, followed by complete disappearance of the symptoms in a further 1–2 days in the majority of cases. There were no serious toxic reactions.

J. G. Dumoulin

53. The Action of Chloropromazine (Largactil), Bromopromazine and Fevoropromazine on the Fallopian Tubes in vitro. (Wplyw Largaktylu oraz fluoro i Bromo-Promazyny na izolowany jajowod ludzki.)

By A. BIELECKI and S. KURZEPA. *Ginek. pol.*, **31**, 275–279, 1960. 1 fig. 14 refs.

The author investigated the action of phenothiazine derivatives such as Largactil, Bromopromazine and Fluoropromazine on the Fallopian tubes *in vitro*. He noticed that the above group of drugs had a paralytic effect on the muscle of the tube with a prolonged disappearance of spontaneous contractions and dilatation of the lumen. On the basis of this observation he suggests the use of these drugs in hysterosalpingography.

S. H. Riterband

54. Interadnexal Hysterectomy with Preservation of Pediculated Endometrial Flap and the Treatment of Multiple Fibroids of the Uterus.

By P. SIRBU, I. BUTNARU and V. PANSCU. *Obstet. si Ginec.*, pp. 67–71, Jan. 1960. 7 figs. 7 refs.

In young women with multiple uterine fibroids the authors advise this type of operation as they believe that the endometrium has an endocrine function. They suggest that this operation should be carried out where myomectomy is not practicable in women under 40 years of age. They describe the technique of this operation whereby most of the tumours are removed by a subtotal hysterectomy, leaving a flap of the endometrium, which will subsequently show menstrual function. They believe that the operation preserves the synergism between uterus and ovaries.

The contra-indications to this operation are: (*a*) Infection of the adnexa. (*b*) Pyometritis. (*c*) Suspicious lesions of the cervix. (*d*) Degenerated fibroids. (*e*) Fibroids of the cervix.

They have operated on 10 cases without any post-operative complications. The patients have been followed up for at least a year, and they have menstruated regularly, have had no abdominal pains and no sexual disturbances.

Sylvia Lerer

55. The Frequency of Sagittal Myomectomy and Its Results Compared with Other Methods of Surgical Intervention for Uterine Fibroids.

By E. ABUREL and C. JACOB. *Obstet. si Ginec.*, pp. 63–67, Jan. 1960. 1 fig.

In 1954 Professor Aburel published his first article on sagittal myomectomy. His reasons for doing this type of myomectomy were:

(*a*) It does not interfere with the blood vessels and nerves of the ovaries.

(*b*) It preserves almost entirely the endometrium.

(*c*) It preserves the myometrium of the lateral walls of the uterus which are well vascularized and innervated by the plexus of the vascular nervous system.

(*d*) It does not damage the Fallopian tubes.

(*e*) It gives good access and a satisfactory suture line.

These authors give the statistics for 5 years for this operation, taken from two large hospitals, and this type of myomectomy was performed in 145 cases (65 per cent of all myomectomies). They have followed up these cases and have found that:

(1) Menses have been regular with a normal loss, except in one case in which persisting menorrhagia required hysterectomy.

(2) There was no dysmenorrhoea or abdominal pain and no urinary symptoms.

(3) Pregnancy occurred in 6 cases. Two of these went to full term and had normal deliveries. The others had to be terminated.

(4) There were no neuro-vascular or endocrine symptoms following this operation.

(5) Pelvic examination revealed a normal shaped uterus of a normal consistency.

(6) There was no mortality.

Sylvia Lerer

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Brown, H. E., and Jones, B. K. (1961): *J. Obstet. Gynaec. Brit. Commonw.*, **2**, 128.

Sampson, P. (1940): *Obstetrics for Midwives*. 2nd edition. Fraser, London. p. 9.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At the meeting of Council held in the College on Saturday, 28th January, 1961, with the President, Mr. A. C. H. Bell, in the Chair, the following was appointed to give a William Blair-Bell Memorial Lecture in 1961: Dr. Philip R. Norris of London.

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